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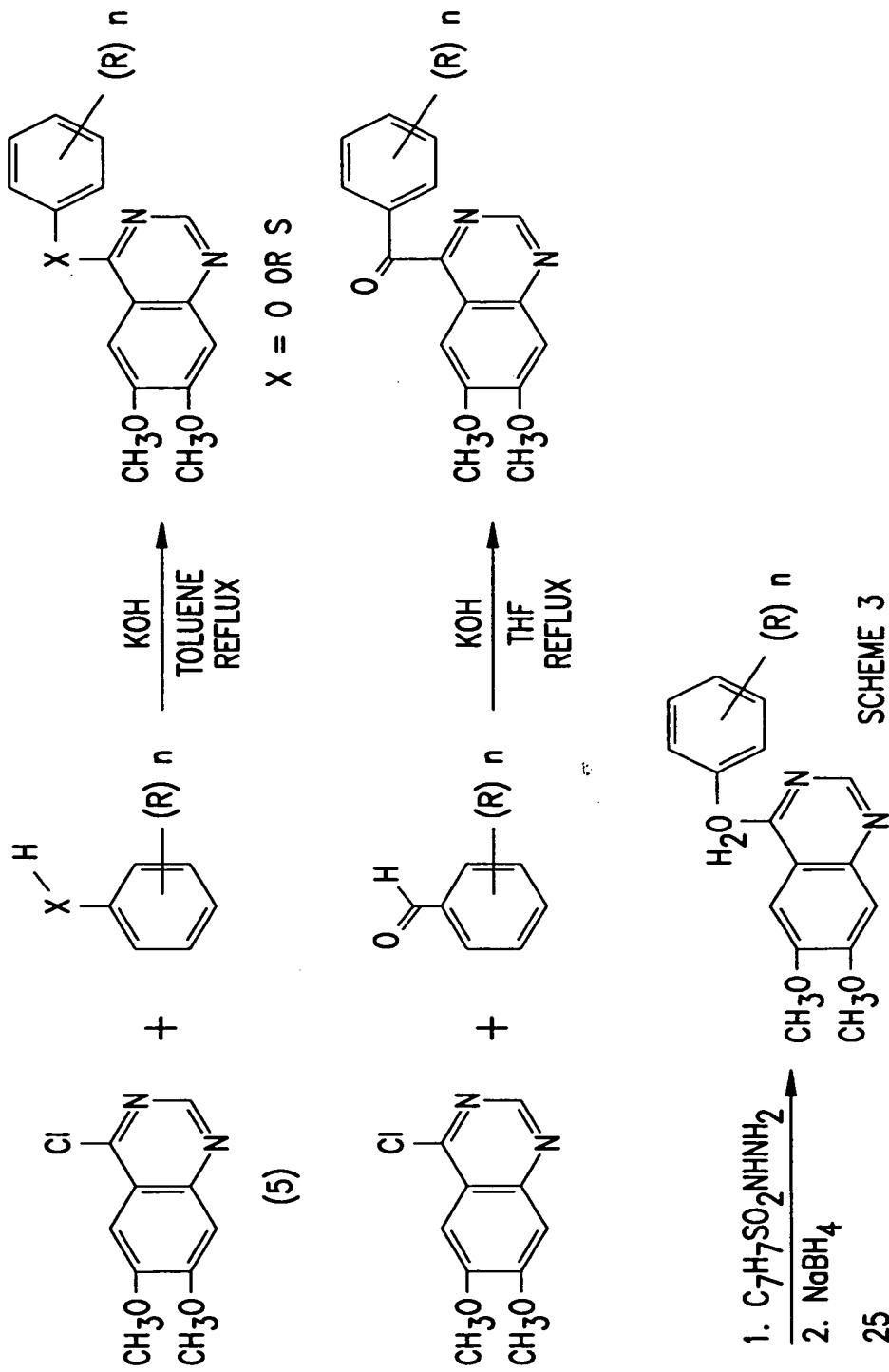
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Inventor: Fatih M. Uckun  
Docket No.: 11669.0054USC4  
Title: THERAPEUTIC COMPOUNDS  
Attorney Name: Denise M. Kettelberger, Ph.D.  
Phone No.: 612.371.5268  
Sheet 1 of 55



1  
FIG.

FIG. 2A

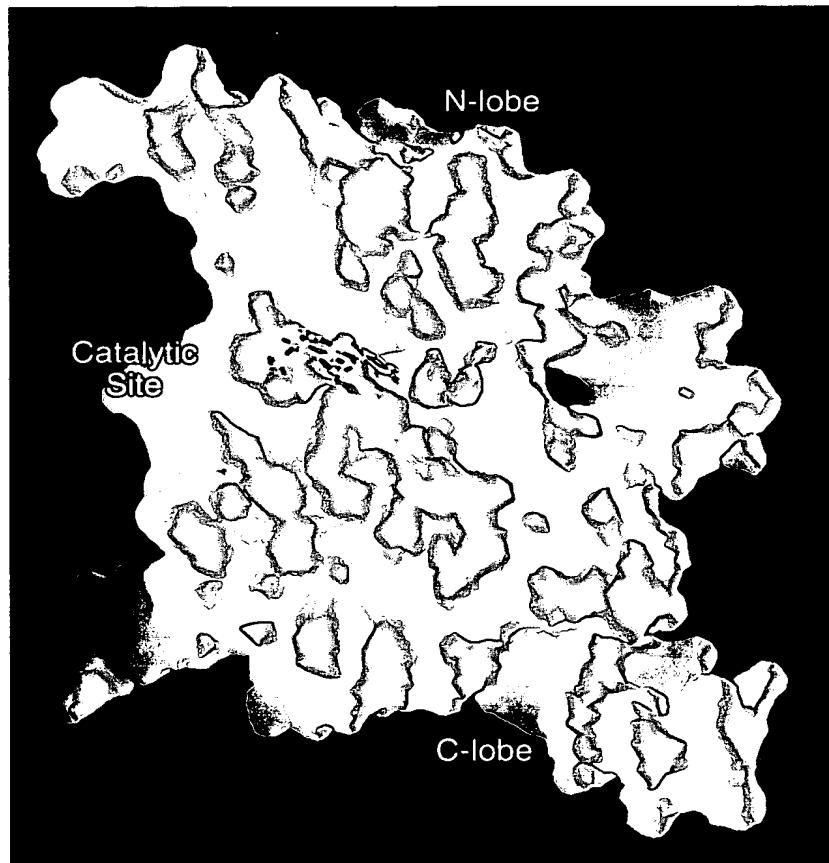


FIG. 2B

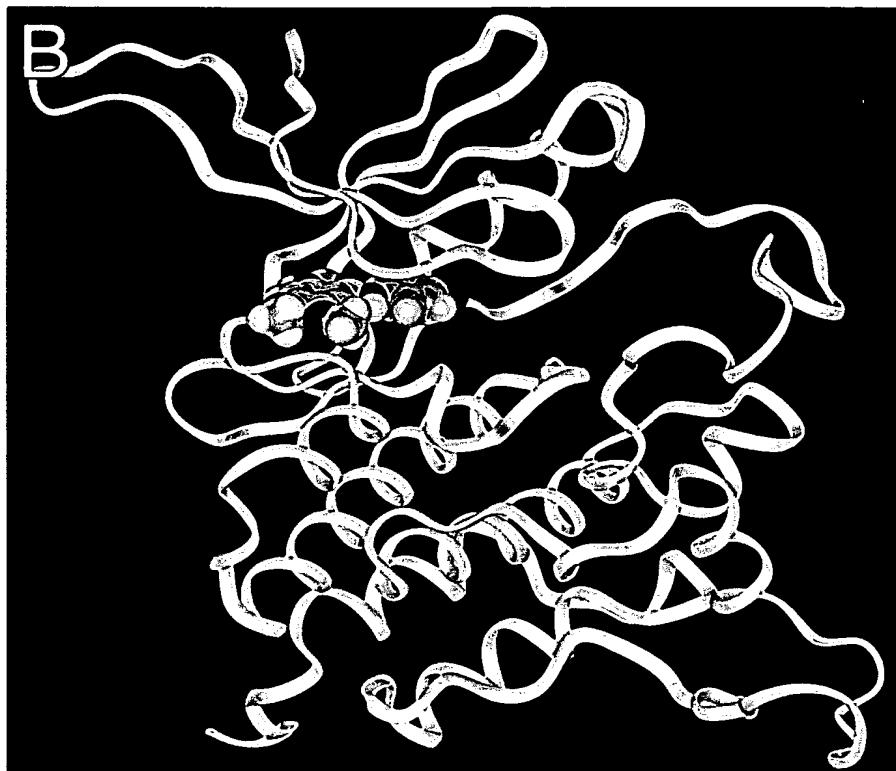


FIG. 2C

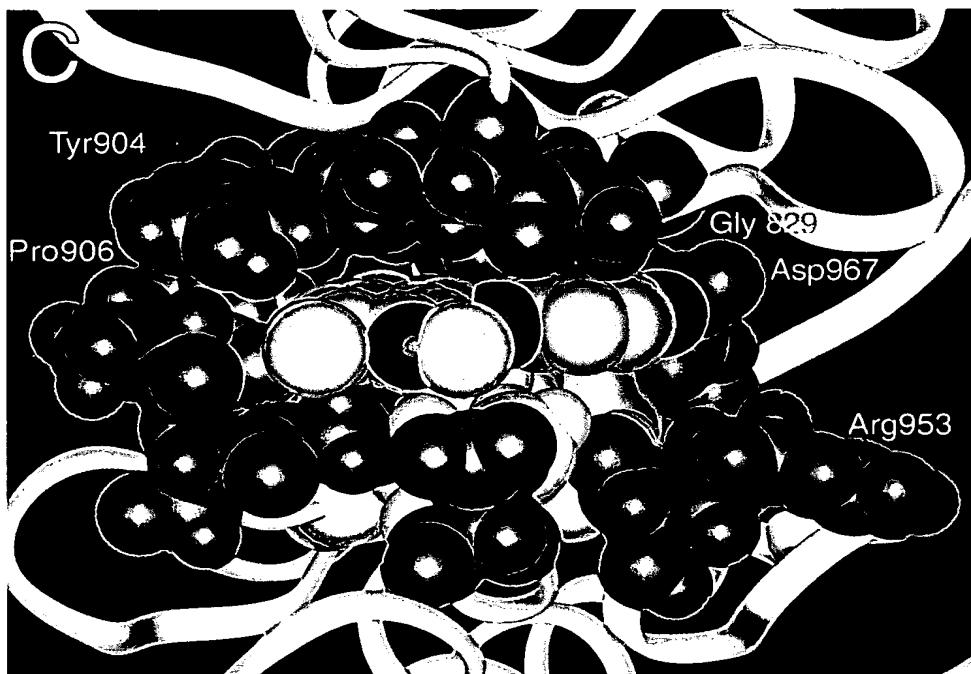


FIG. 3A

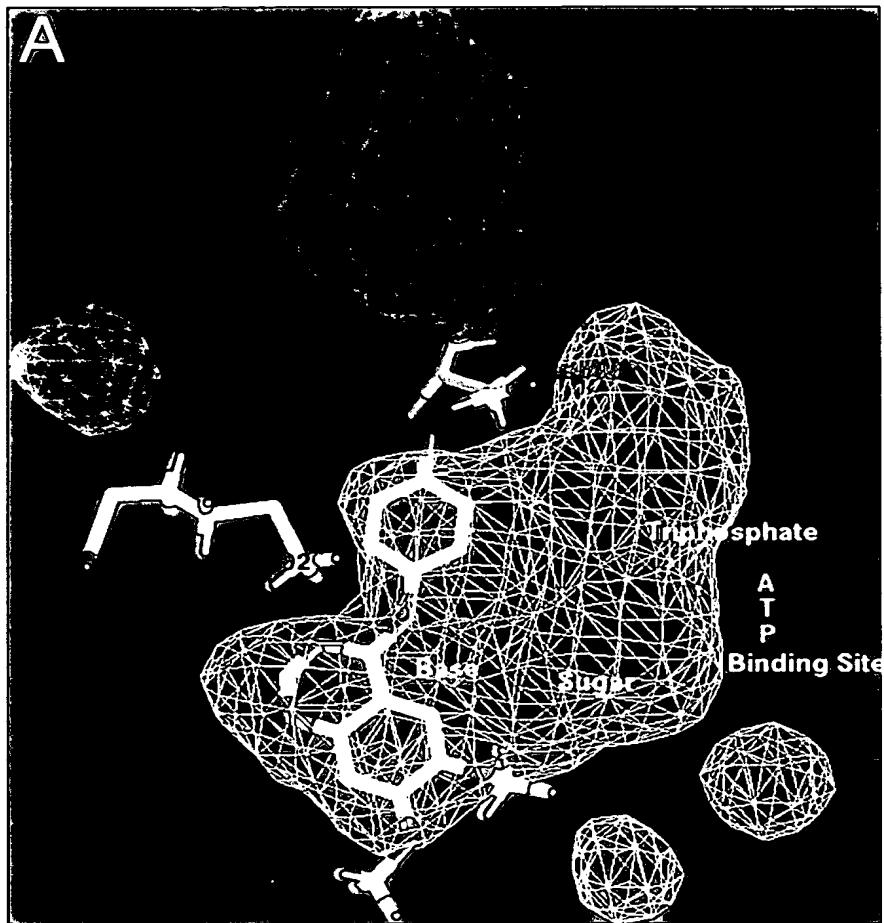
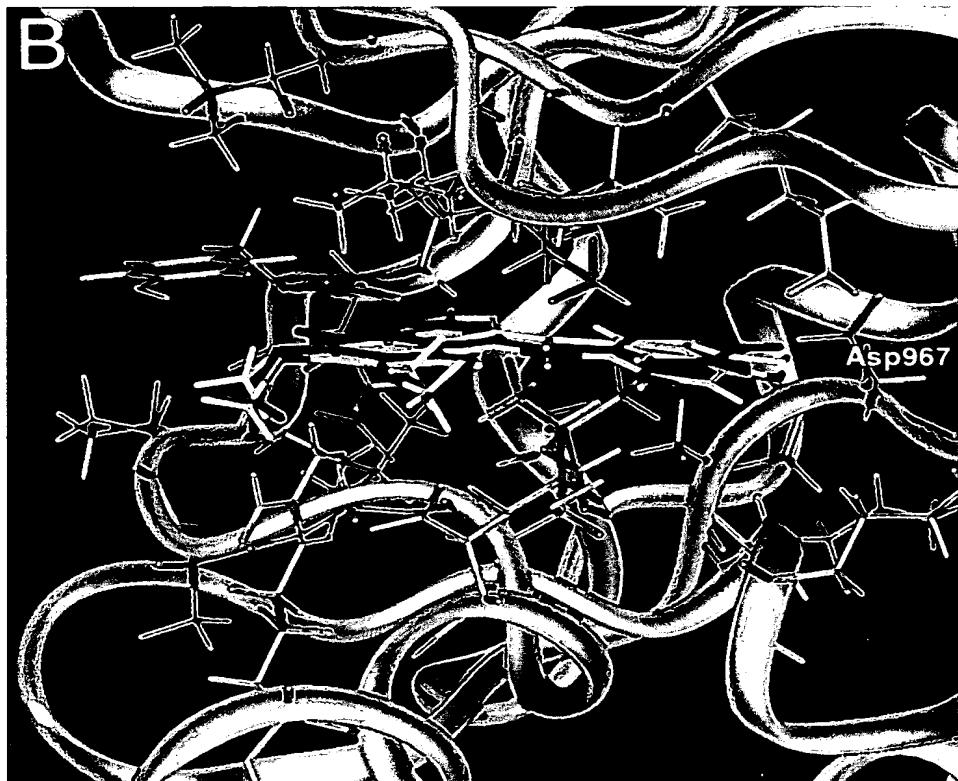


FIG. 3B



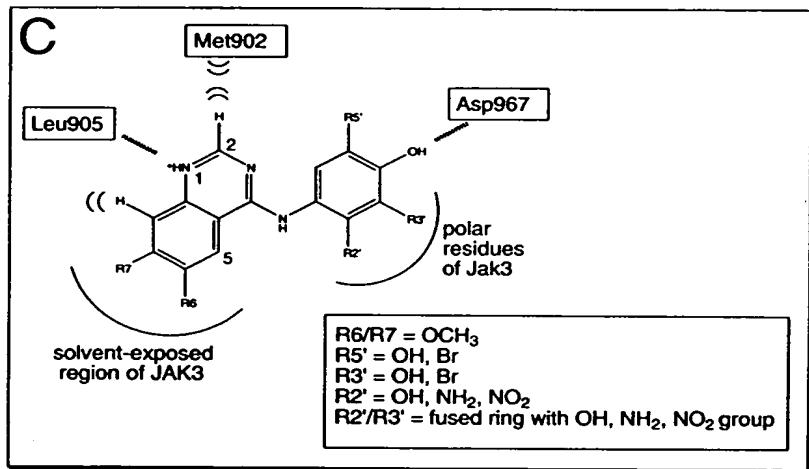
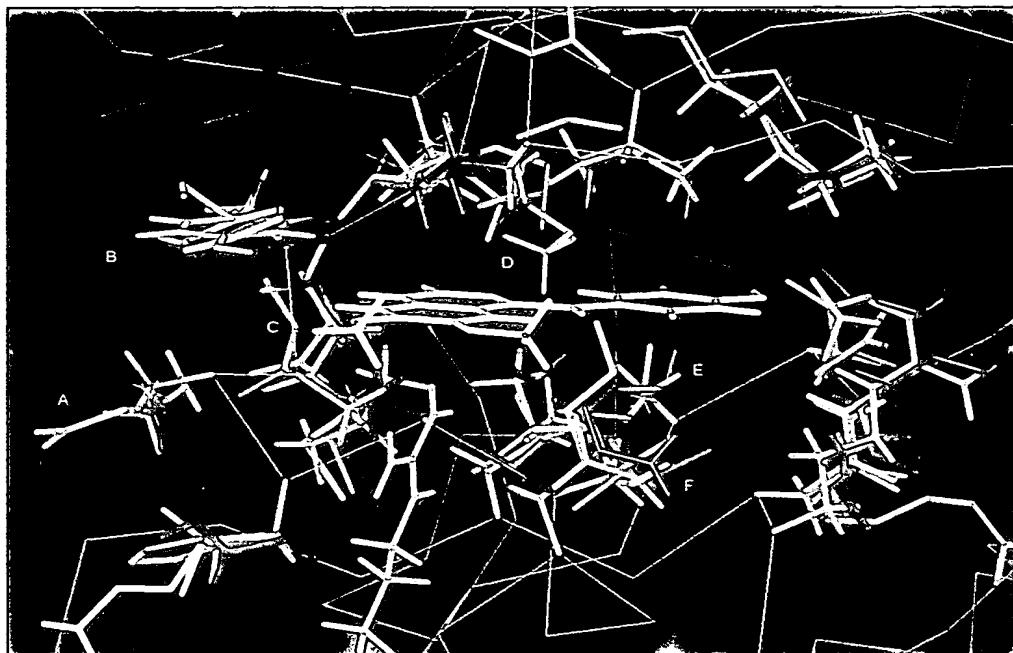


FIG. 3C

FIG. 4A



B

Protein Tyrosine Kinase	Residue at Region A	Residue at Region B	Residue at Region C	Residue at Region D	Residue at Region E	Residue at Region F
JAK3	Pro906	Tyr904	Leu905	Met902	Ala966	Asp912
JAK2	Pro933	Tyr931	Leu932	Met929	Gly993	Asp939
JAK1	Pro948	Phe946	Leu947	Met944	Gly1008	Glu954
BTK	Ala478	Tyr476	Met477	Thr 474	Ser 538	Asn 484
SYK	Glu342	Met340	Ala341	Met338	Ser403	Lys348
HCK	Ala342	Phe340	Met341	Ala342	Ala403	Asp348
LYN	Ala323	Tyr321	Met322	Ala323	Ala384	Asp329
IRK	Ala1080	Leu1078	Met1079	Met1076	Gly1149	Ser1086

FIG. 4B

FIG. 5A

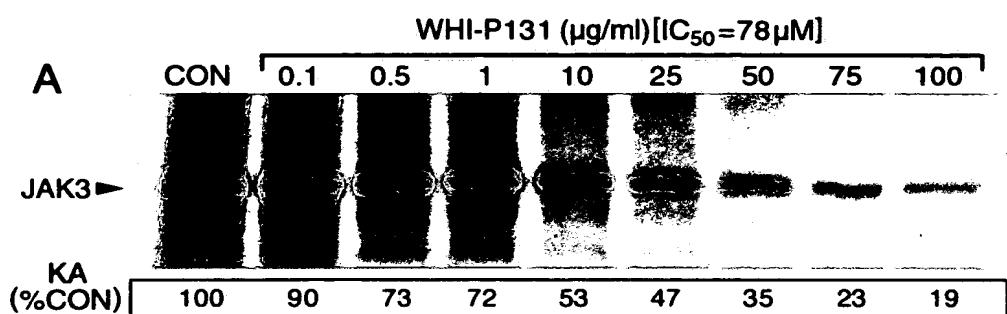


FIG. 5B

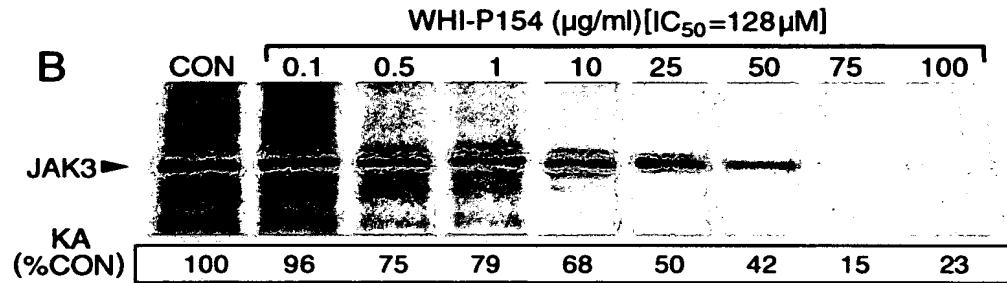


FIG. 5C

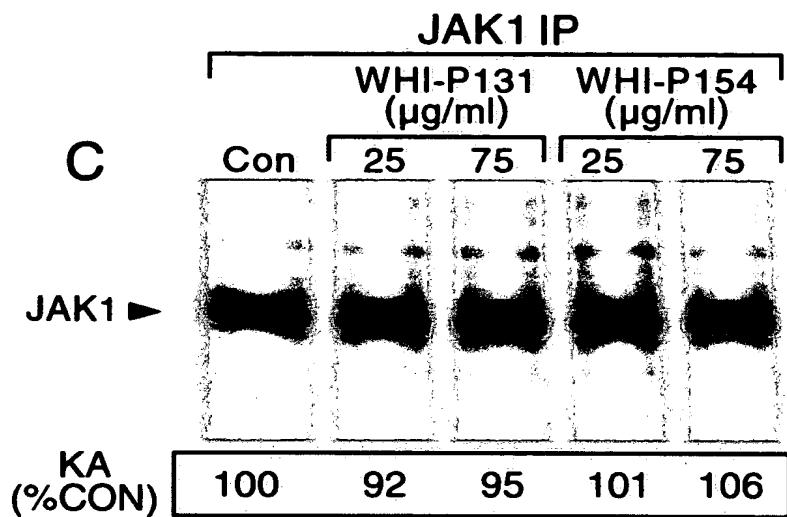


FIG. 5D

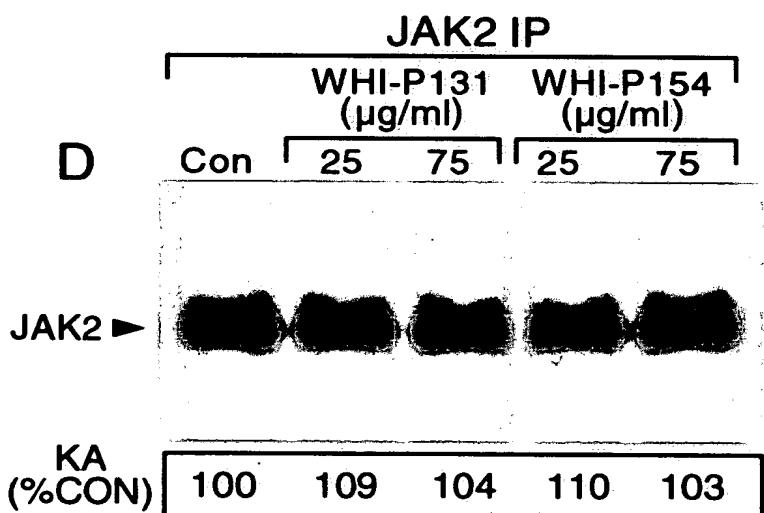


FIG. 5E

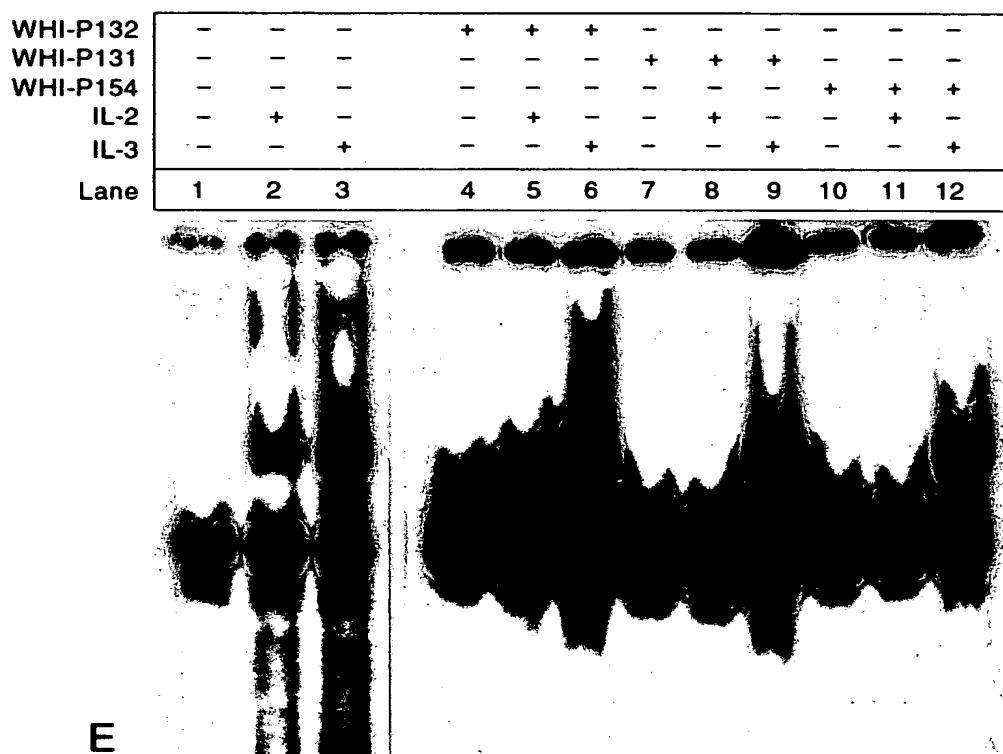


FIG. 6A

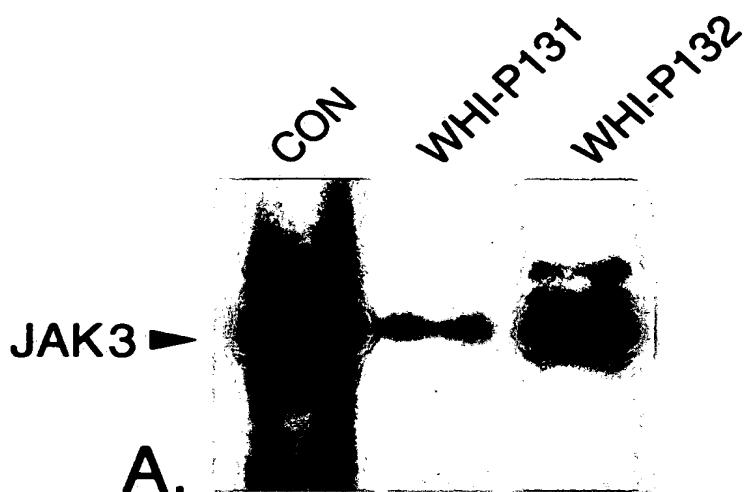


FIG. 6B

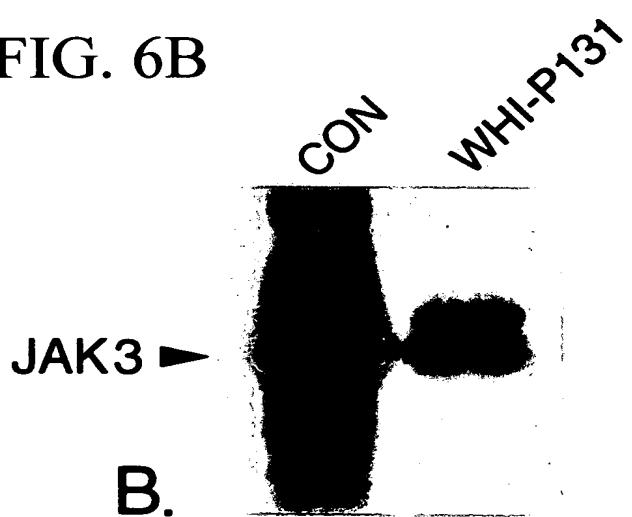


FIG. 6C

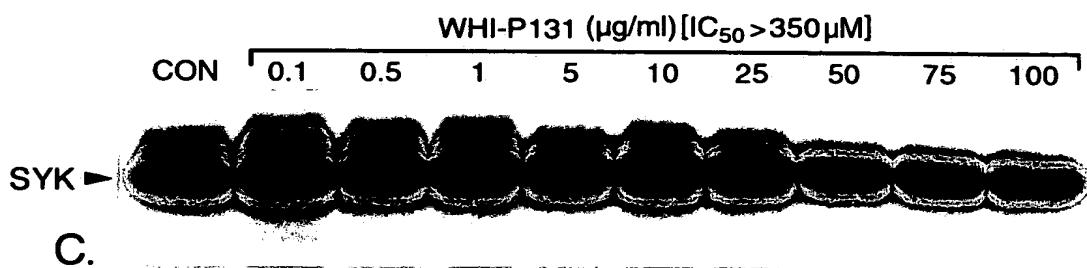
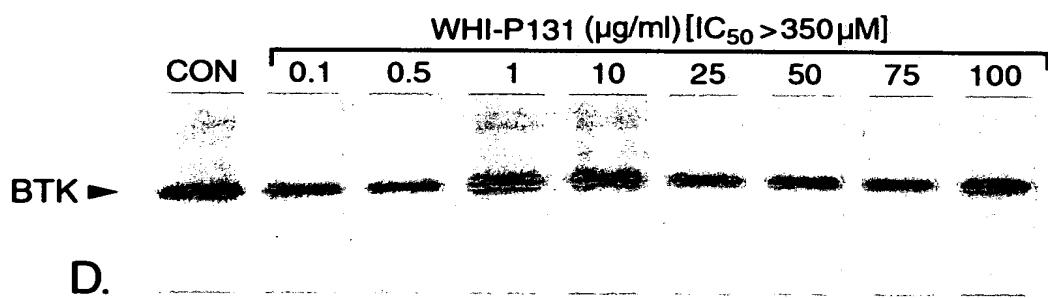


FIG. 6D



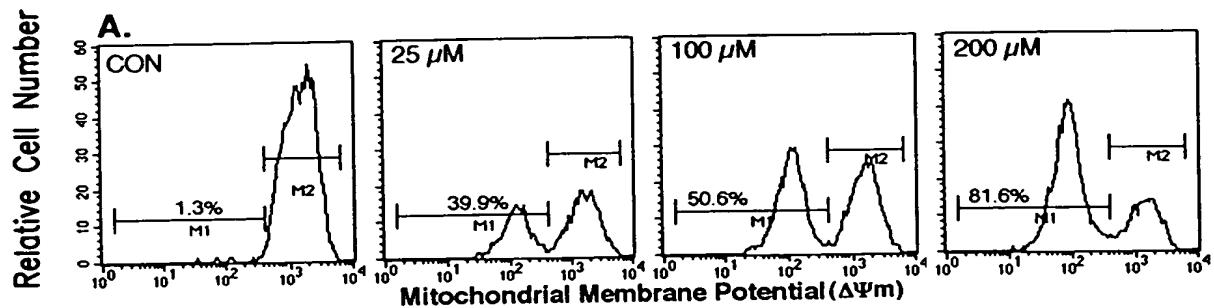


FIG. 7A

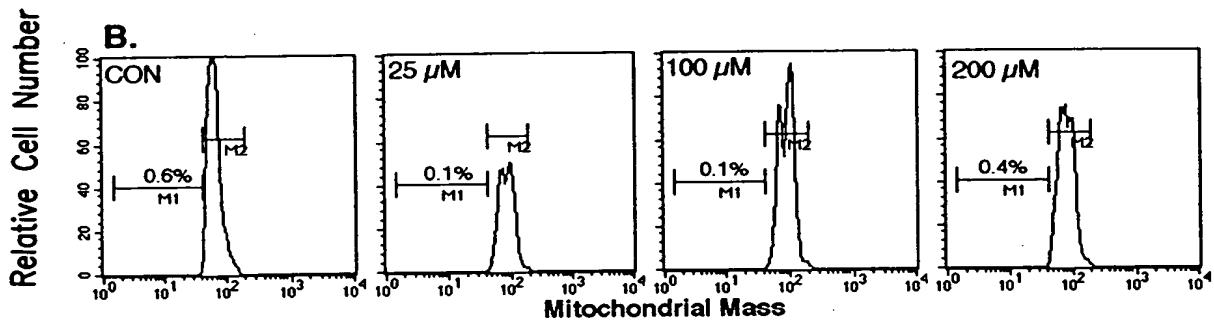


FIG. 7B

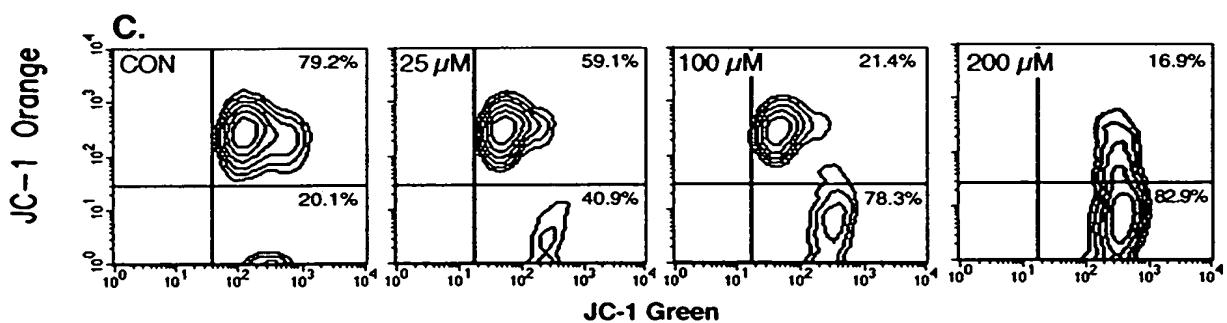


FIG. 7C

FIG. 7D1

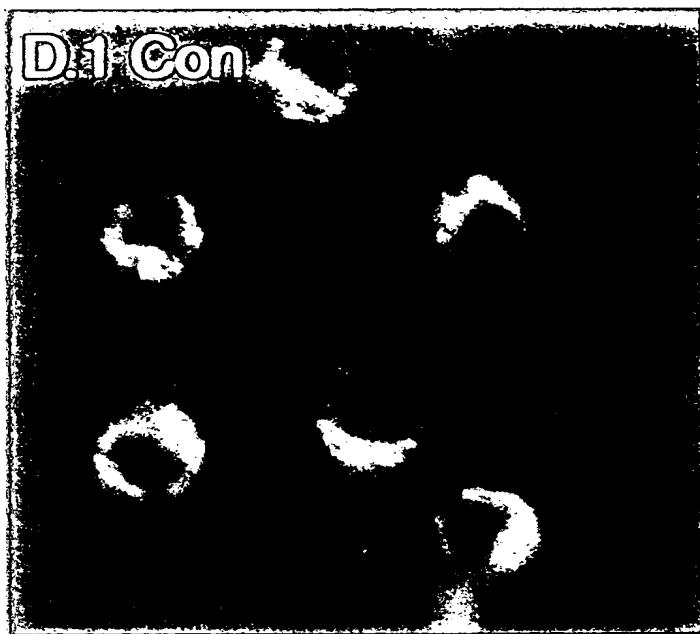


FIG. 7D2



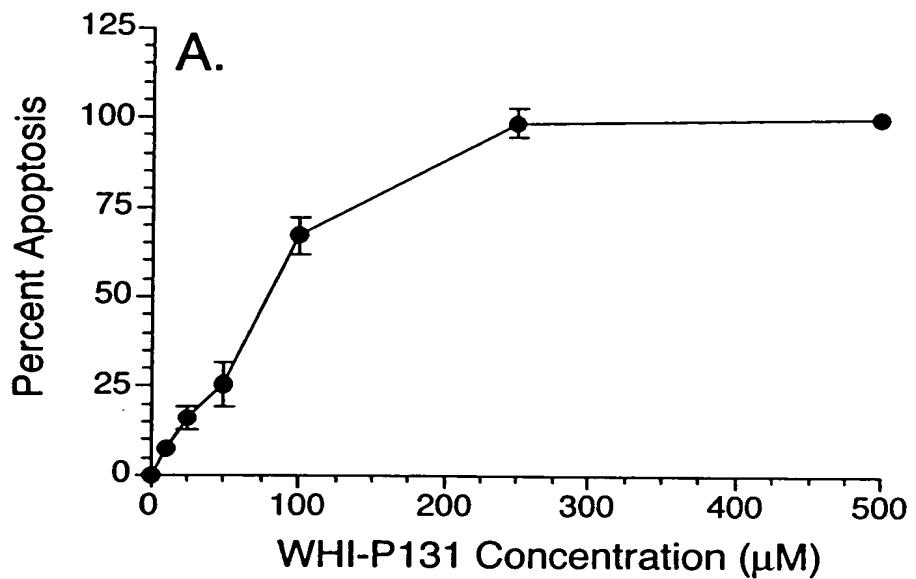


FIG. 8A

}

FIG. 8B1

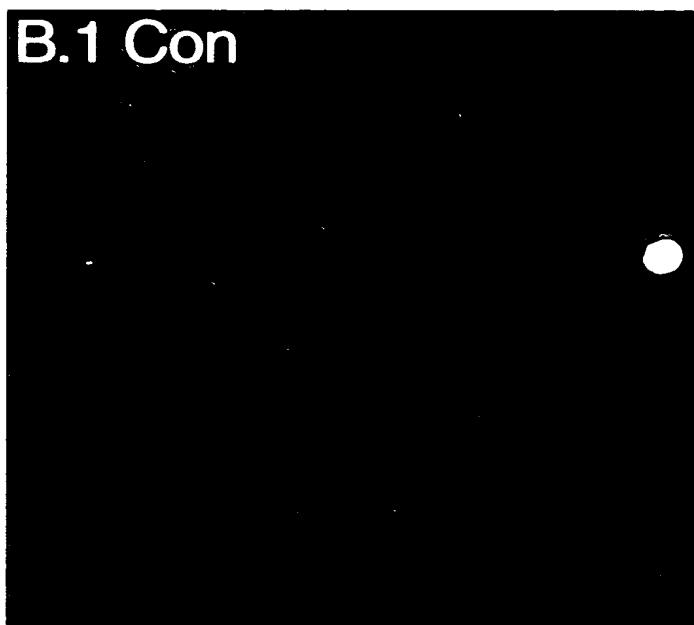


FIG. 8B2

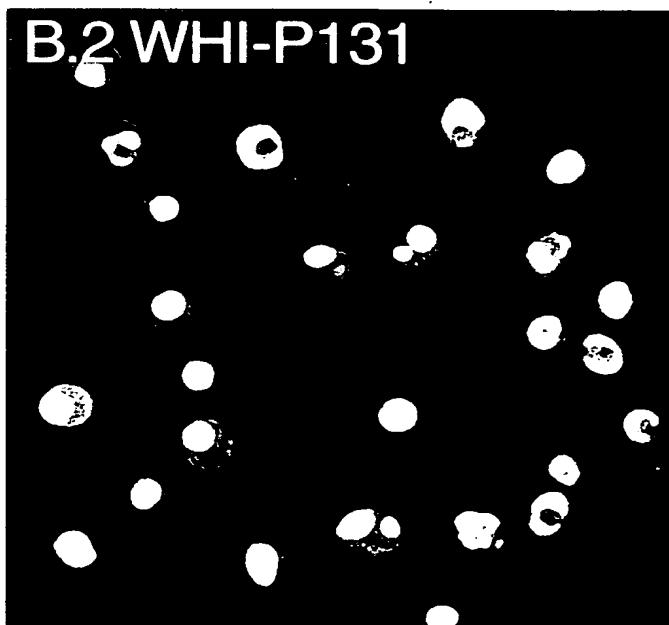


FIG. 9A

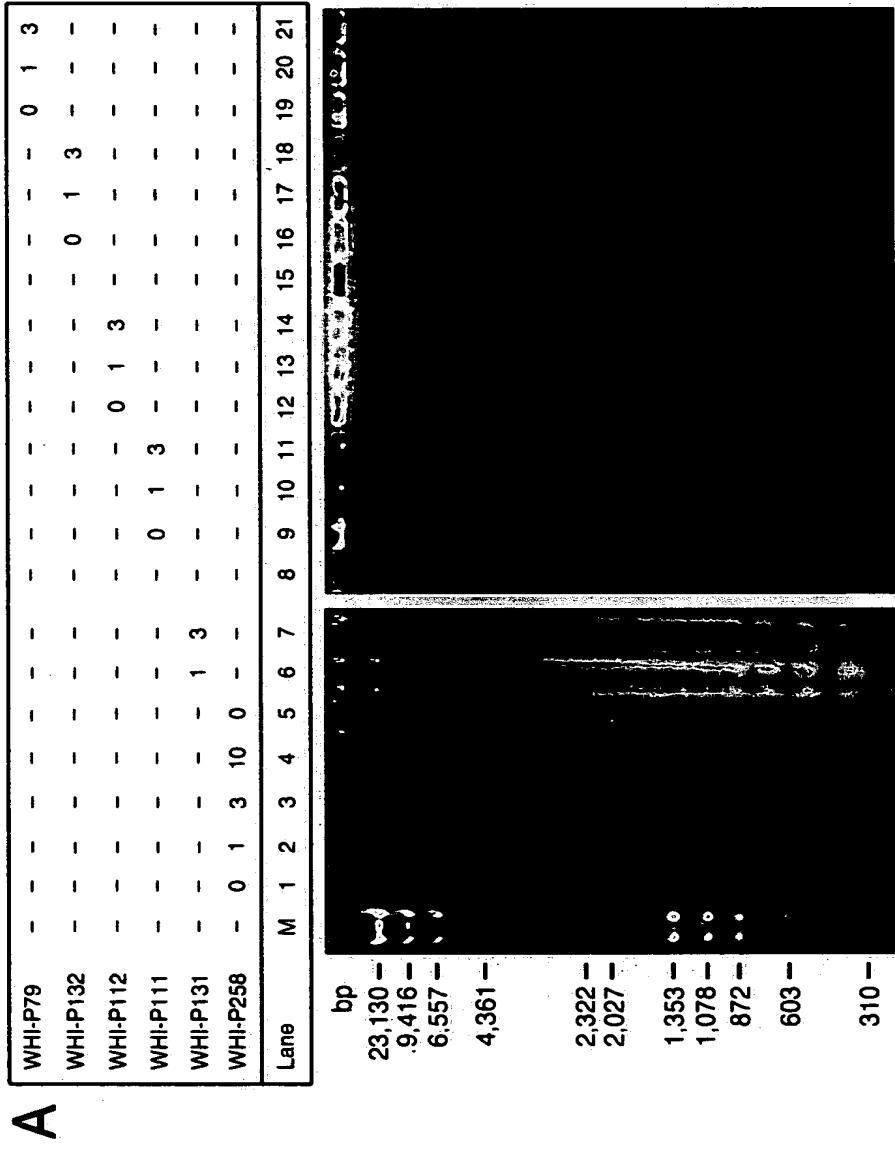


FIG. 9B

B

LCI;19	-	-	-	-	-	-	-	-	-	+	+	+	-
SQ20B	-	-	-	-	-	+	+	+	-	-	-	-	-
M24-MET	-	-	+	+	+	-	-	-	-	-	-	-	-
WHI-P131	-	-	0	1	3	0	1	3	-	0	1	3	-

Lane M 1 2 3 4 5 6 7 8 9 10 11 12

bp

23,130 -

9,416 -

6,557 -

4,361 -

2,322 -

2,027 -

1,353 -

1,078 -

872 -

603 -

310 -



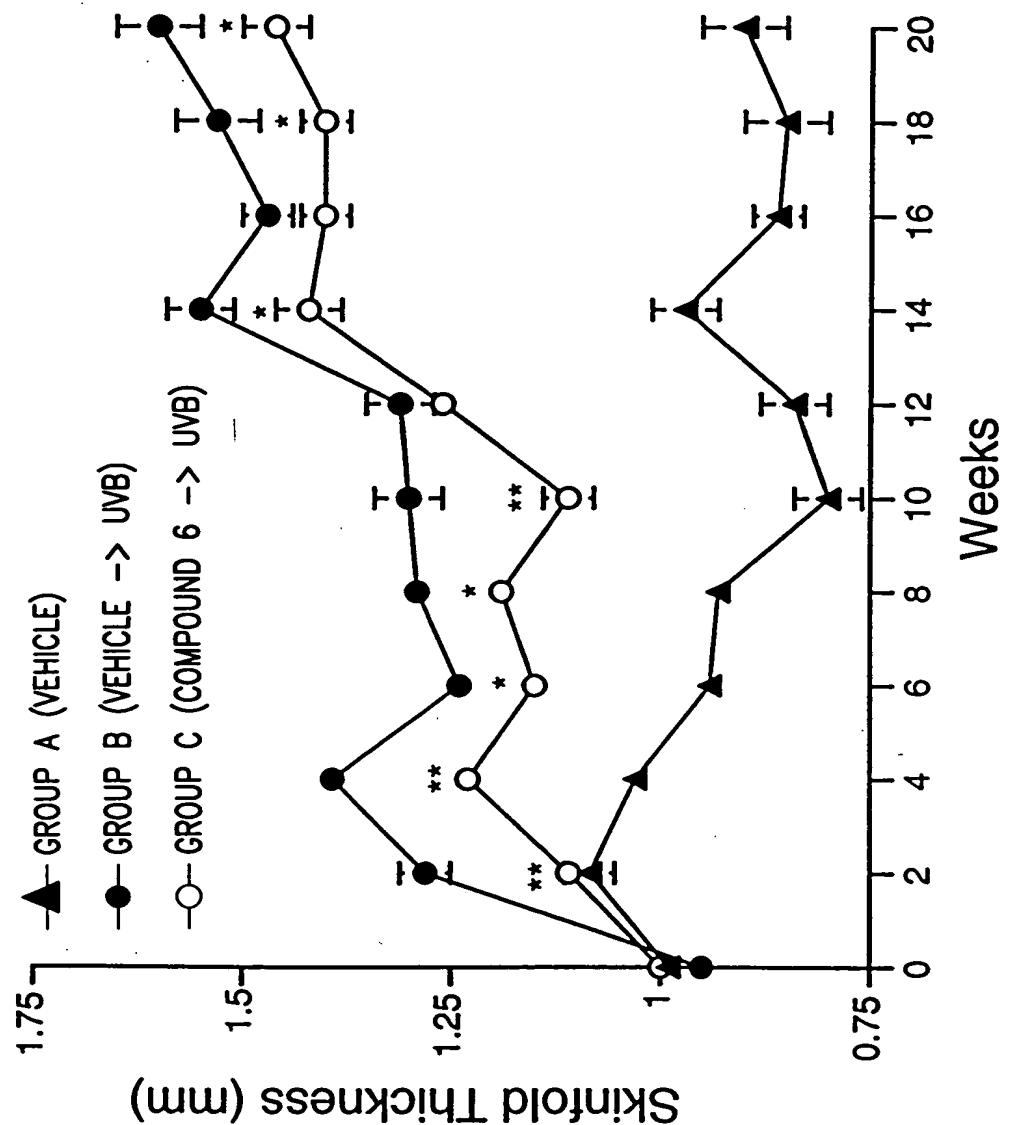


FIG. 10

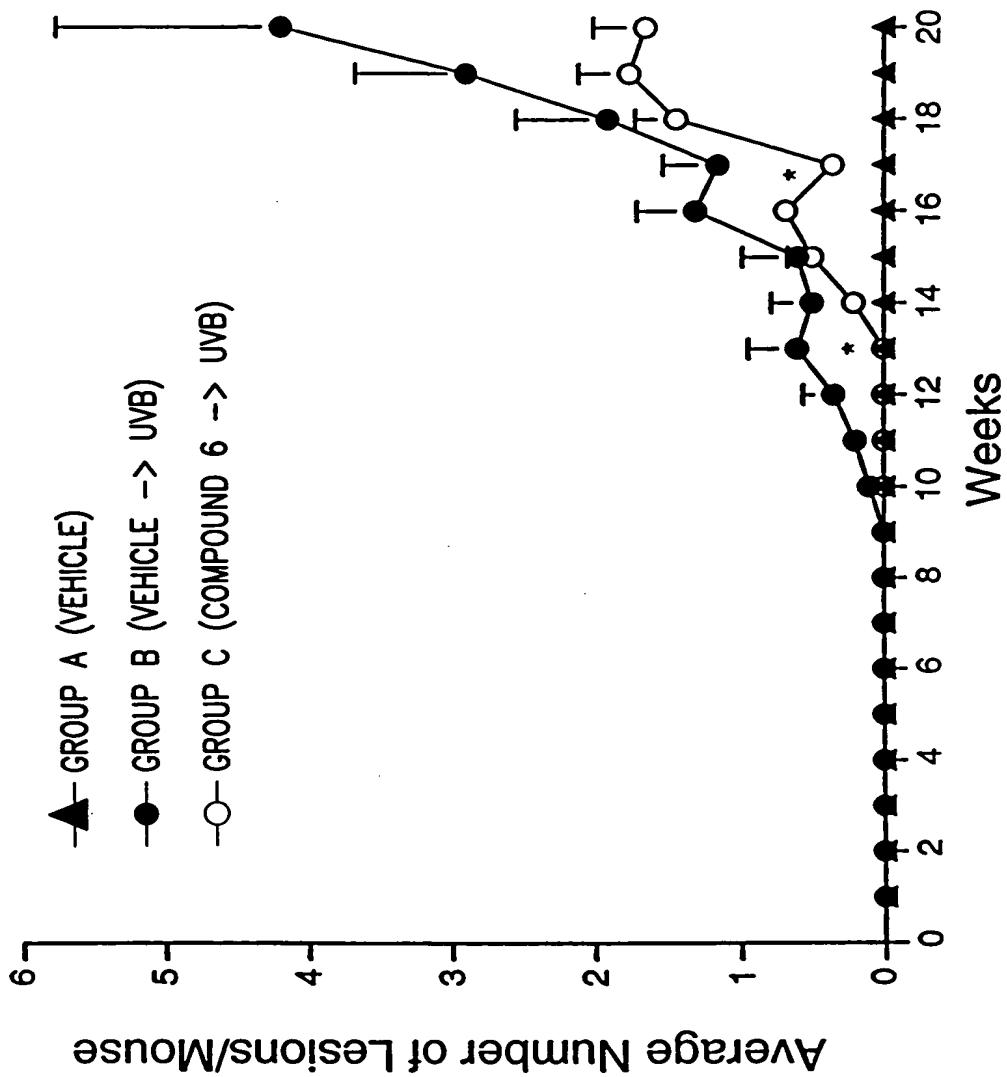


FIG. 11

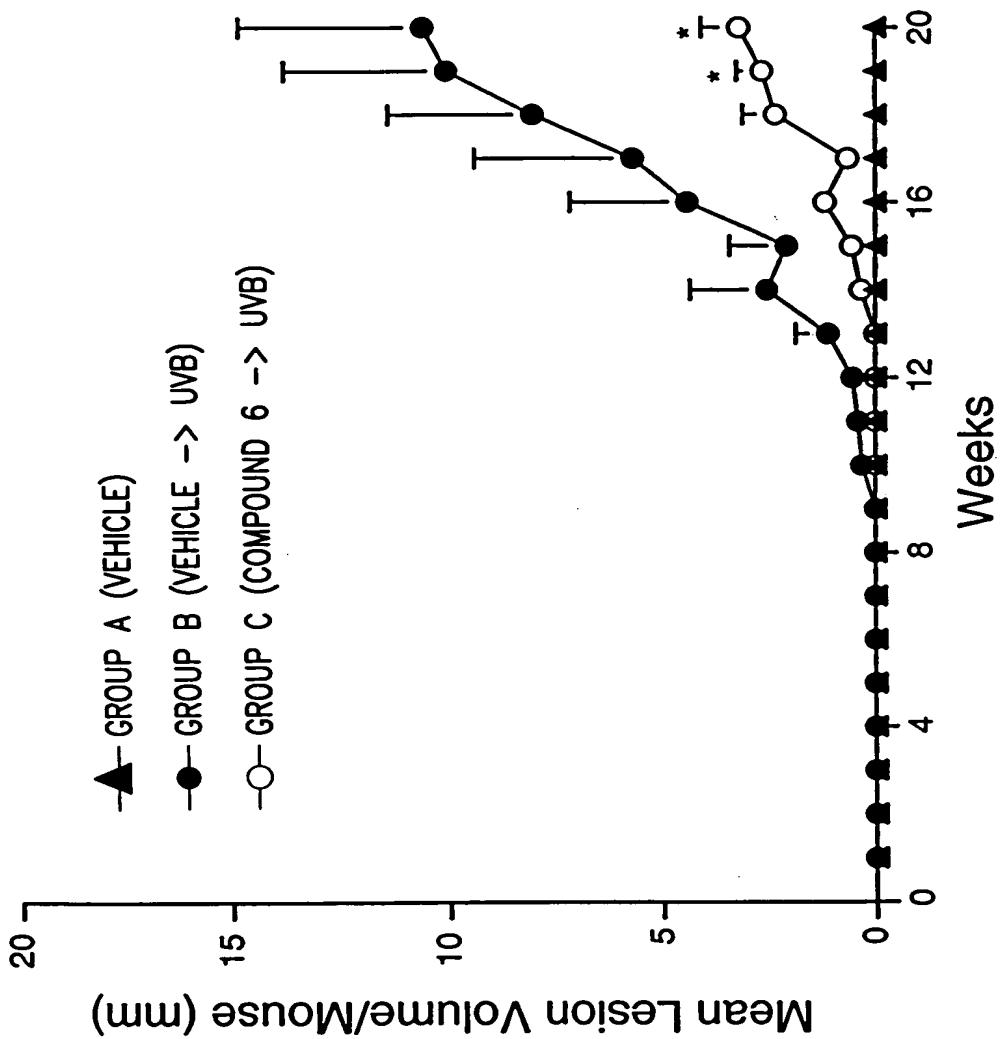
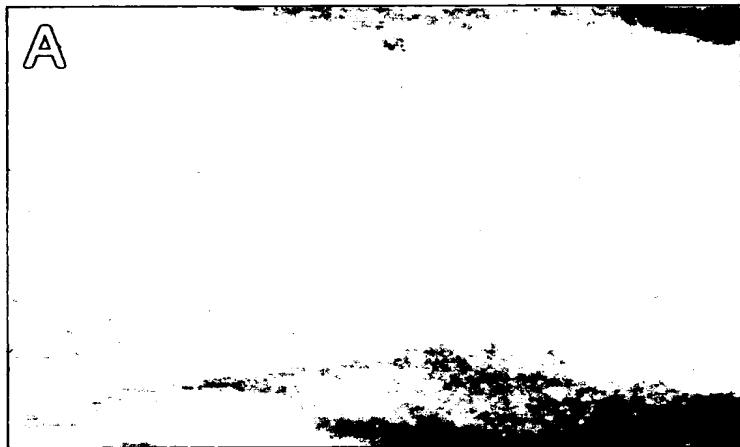
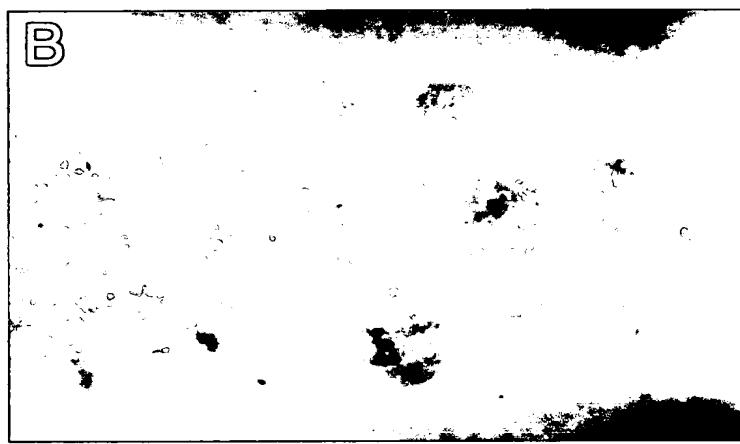


FIG. 12

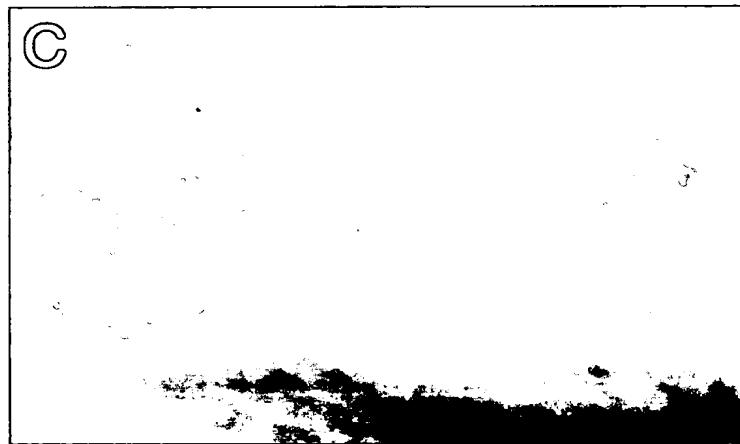
**FIG. 13A**



**FIG. 13B**



**FIG. 13C**



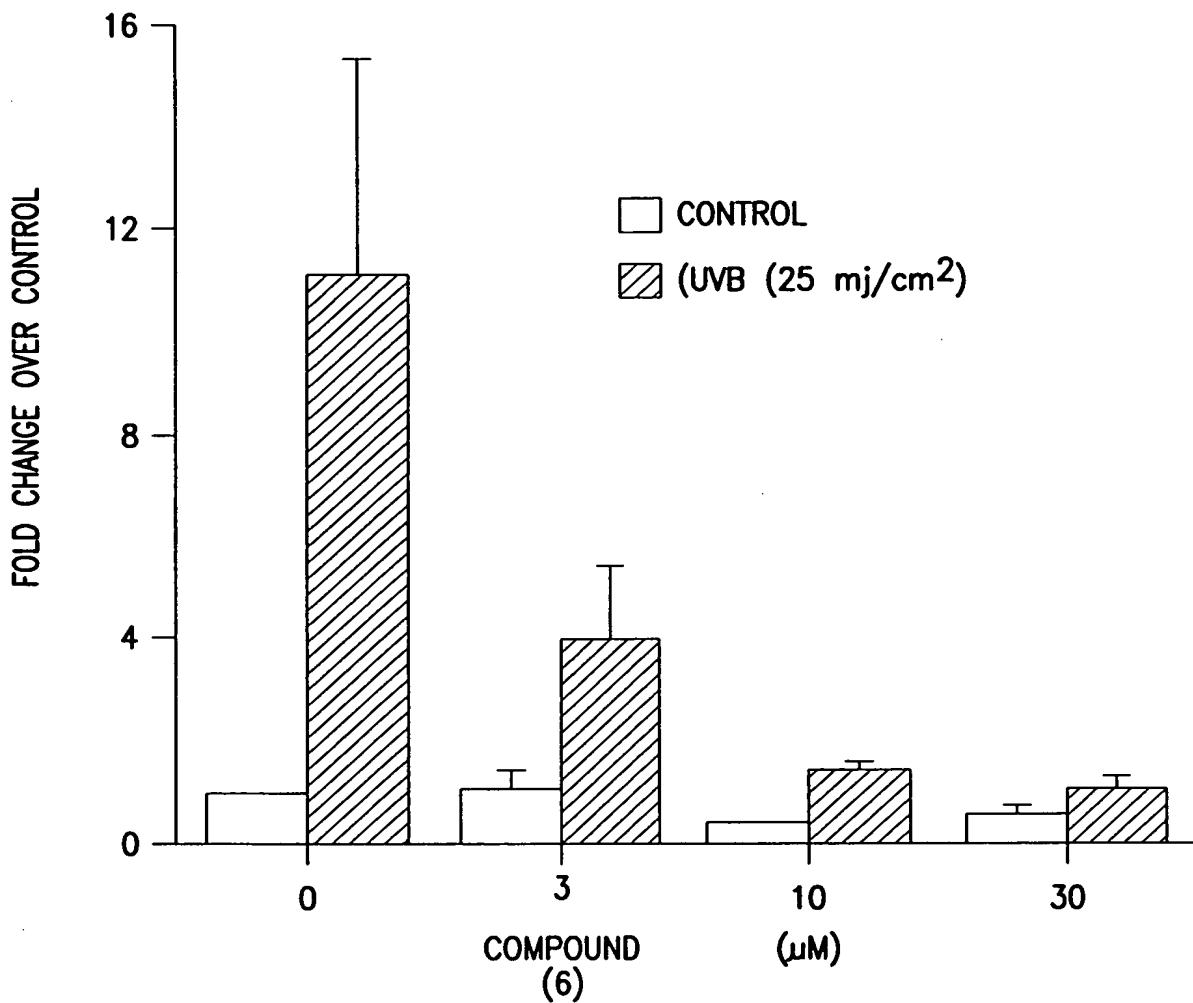


FIG. 14

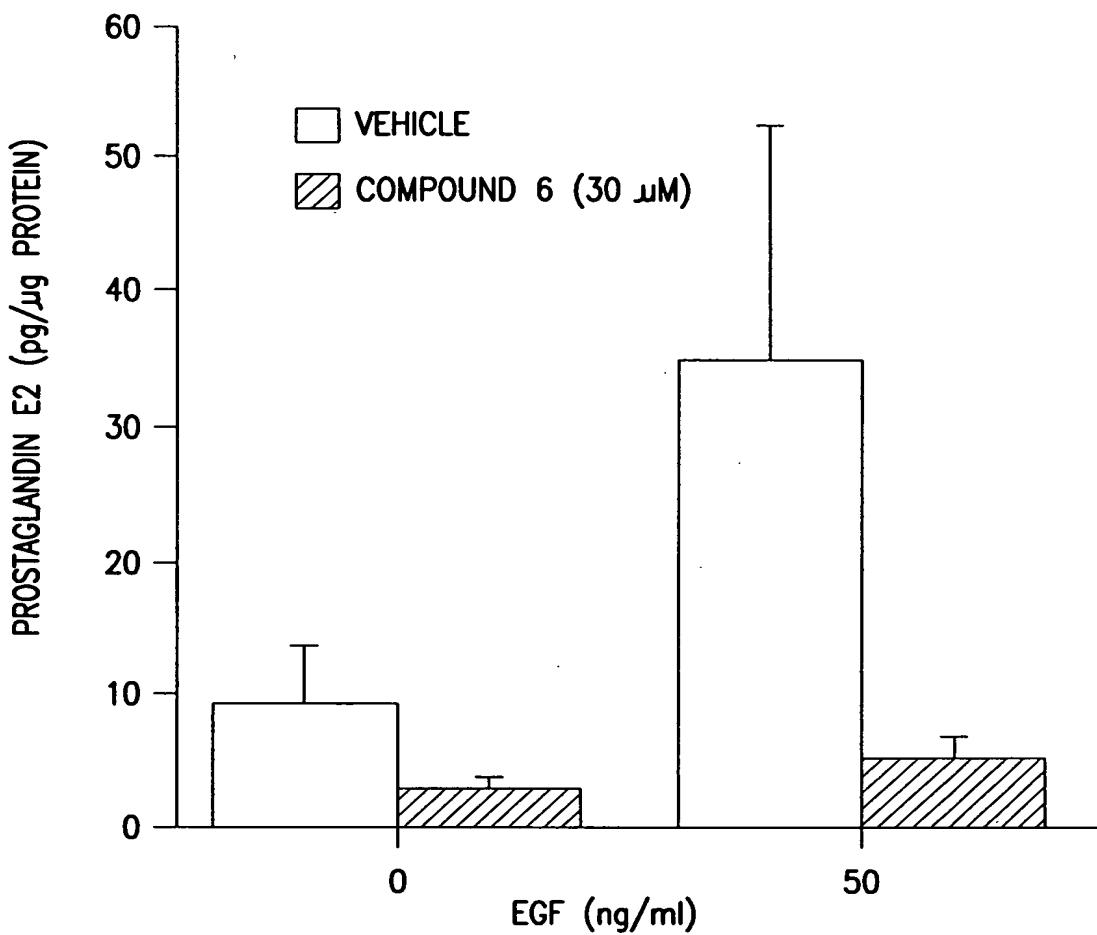


FIG. 15

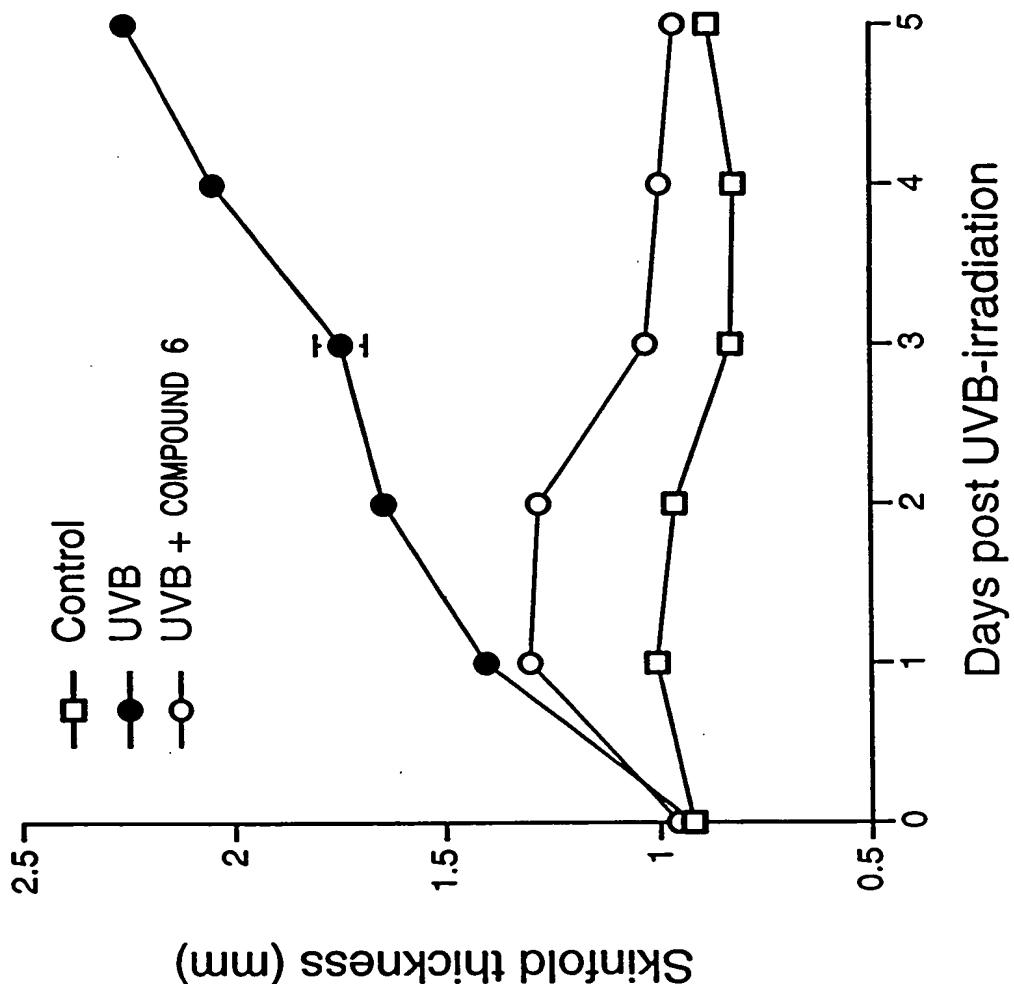


FIG. 16

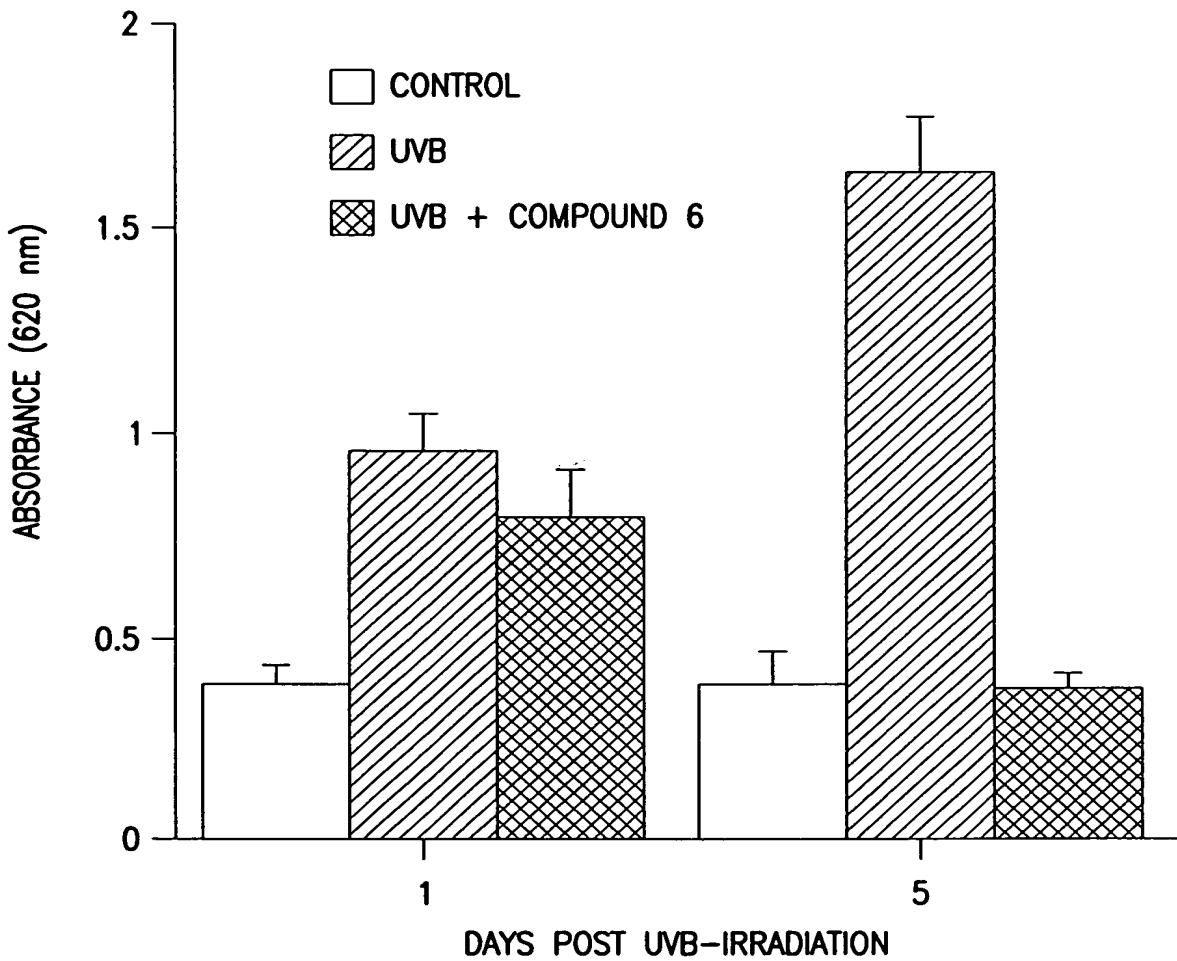
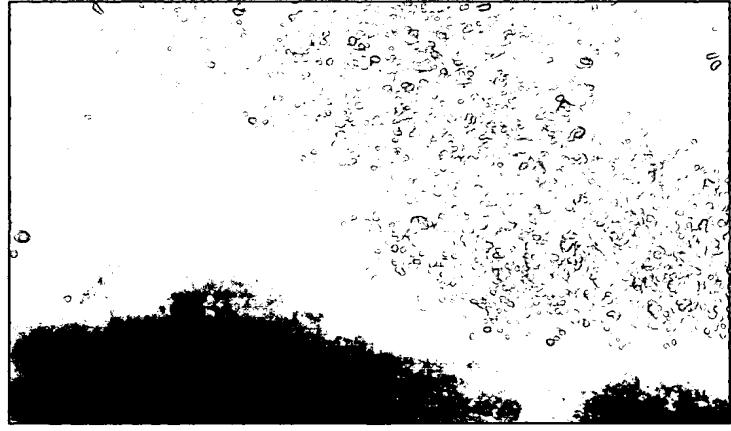


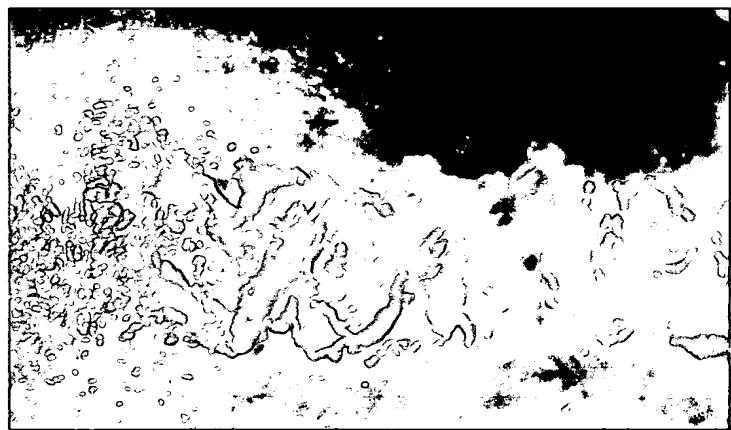
FIG. 17

FIG. 18A



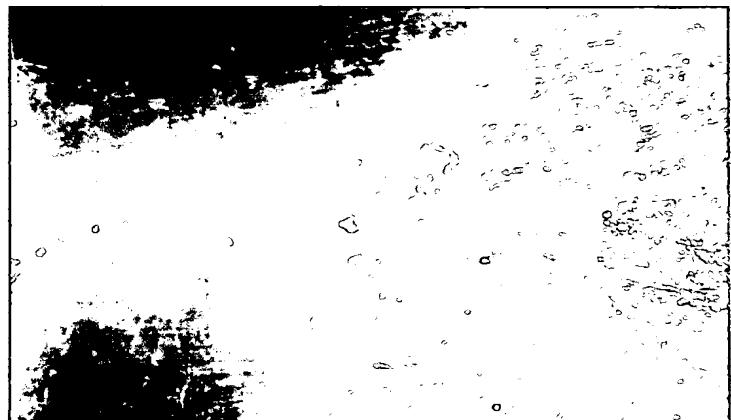
A. Control

FIG. 18B



B. UVB

FIG. 18C



C. DDE9501+UVB

FIG. 19A

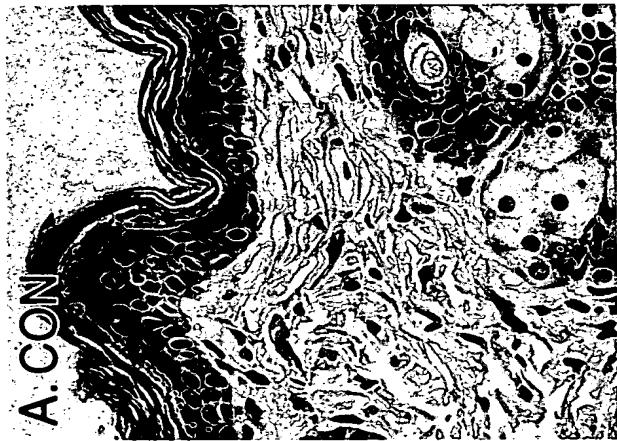


FIG. 19B



FIG. 19C

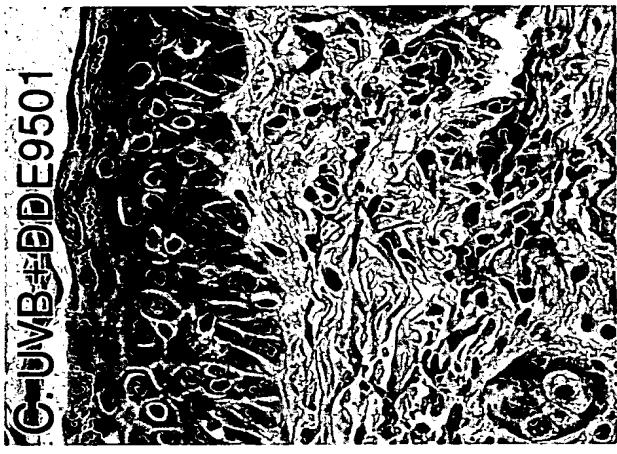




FIG. 20A



FIG. 20B

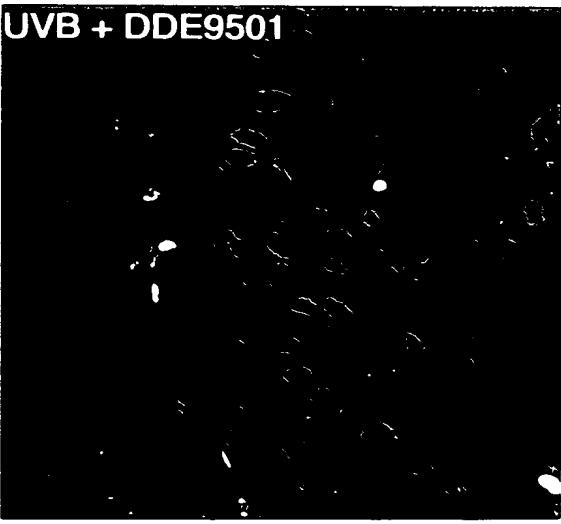


FIG. 20C

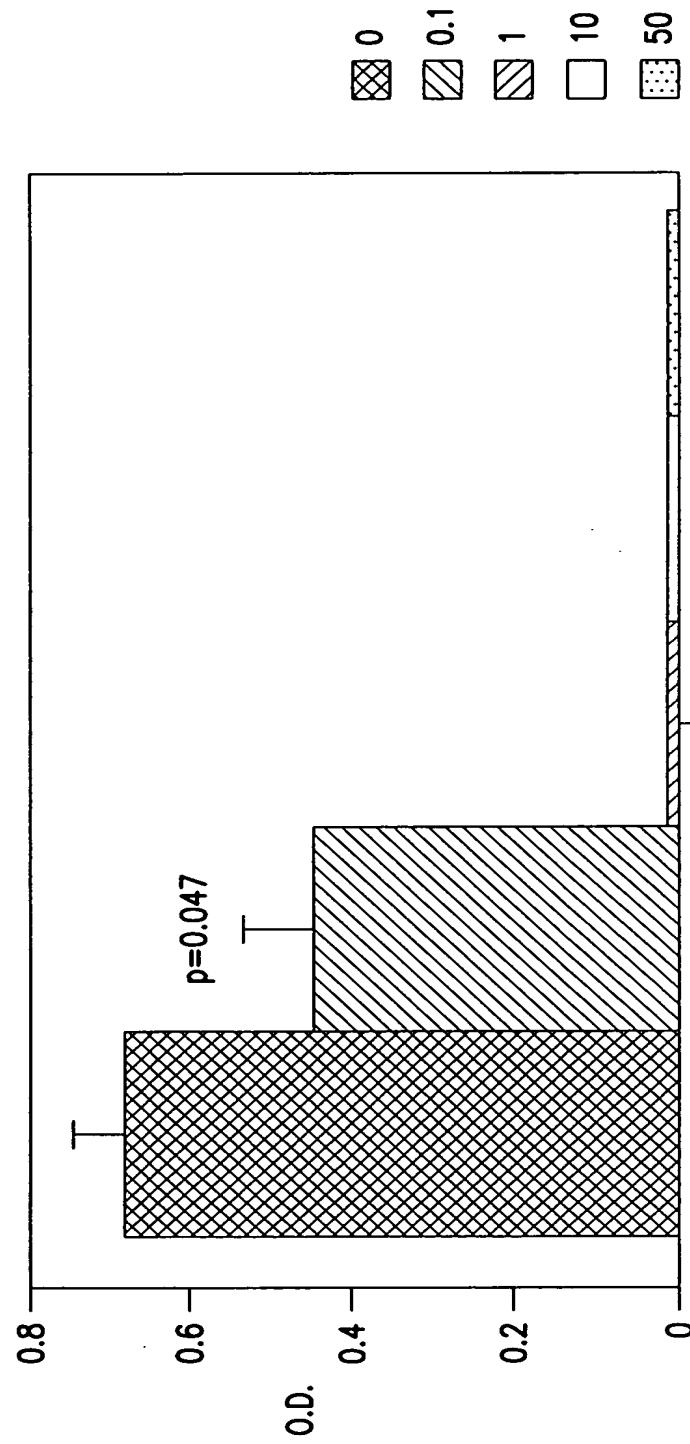


FIG. 21A

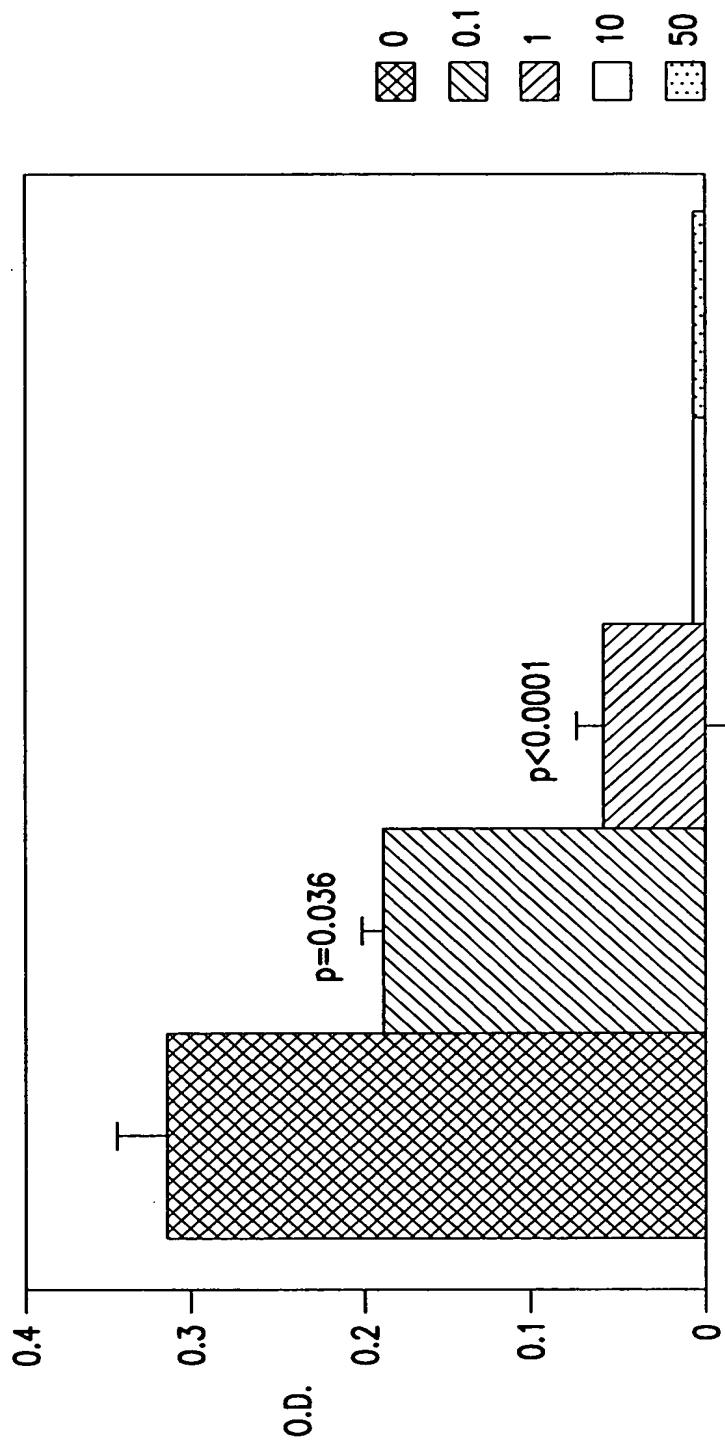


FIG. 21B

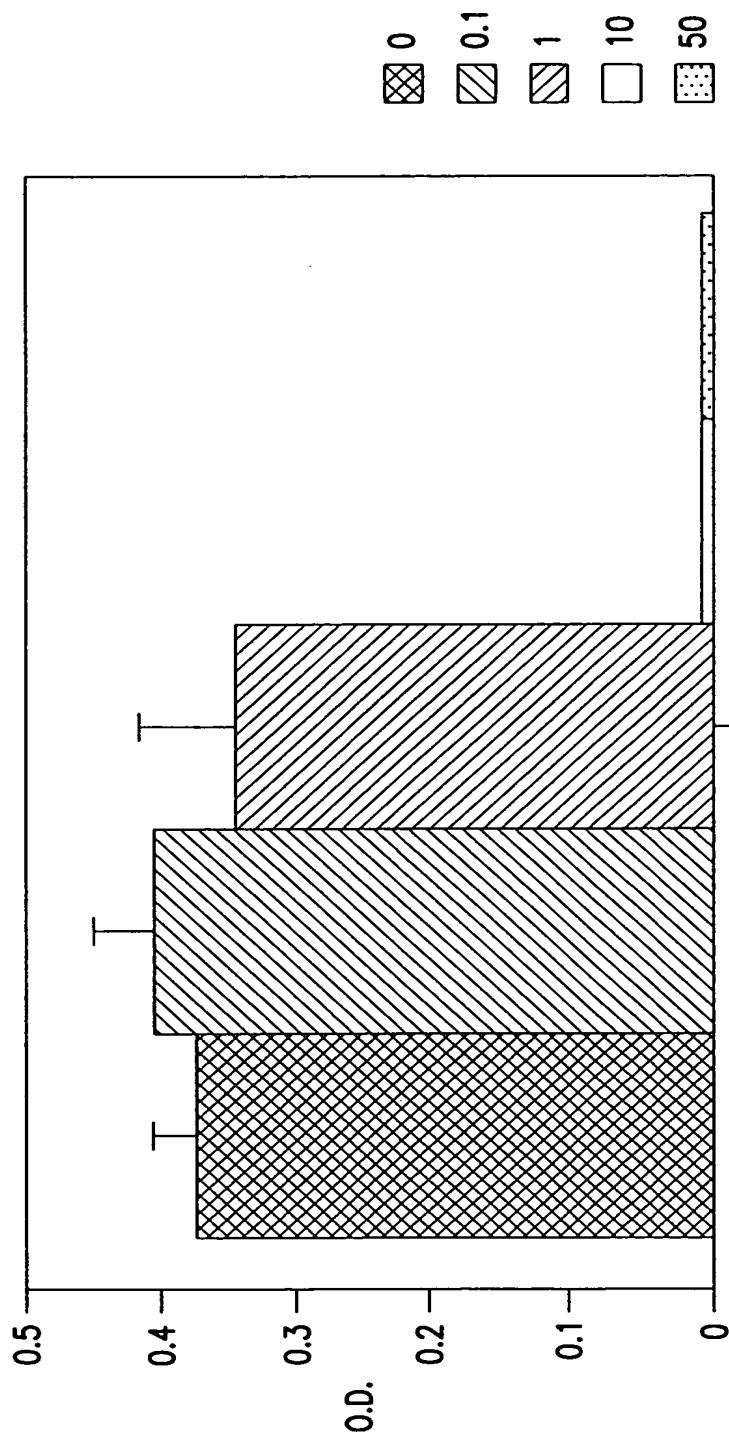


FIG. 21C

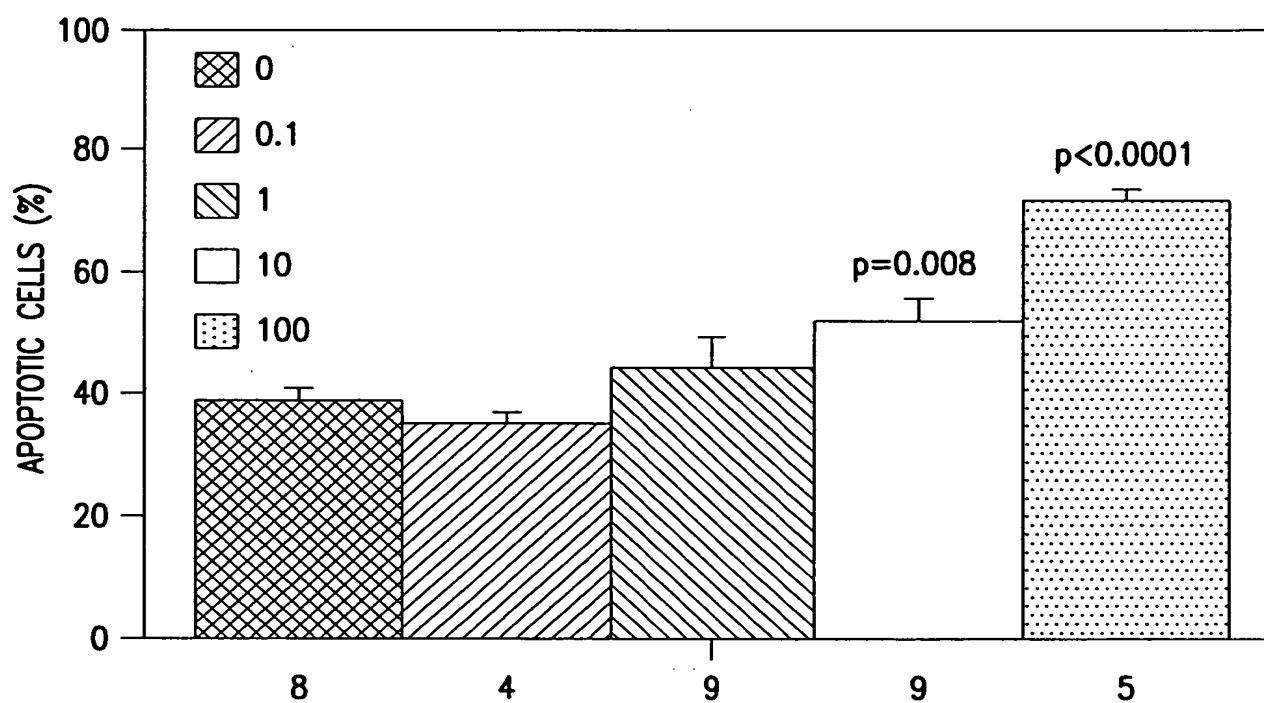


FIG. 22

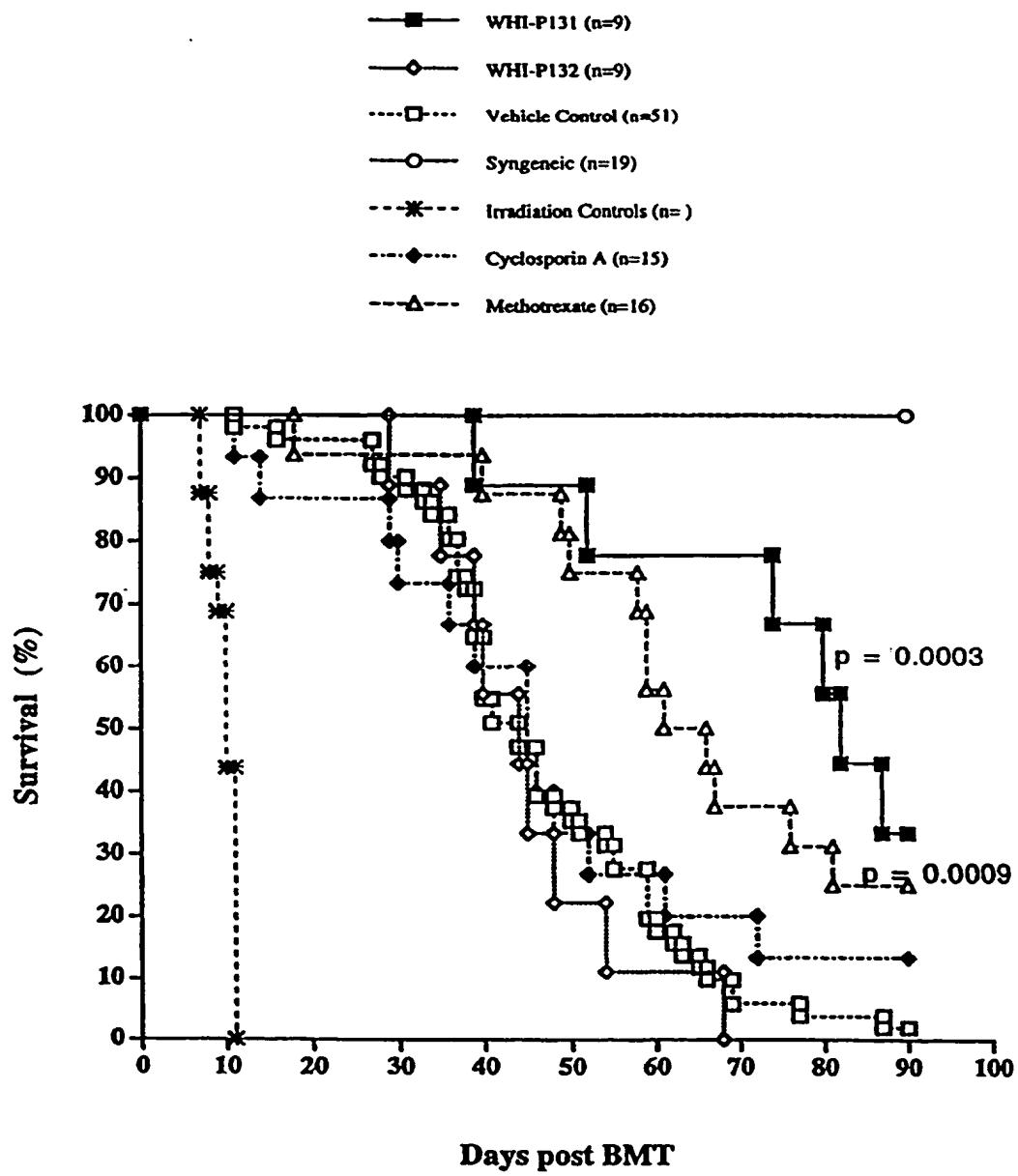


FIG. 23

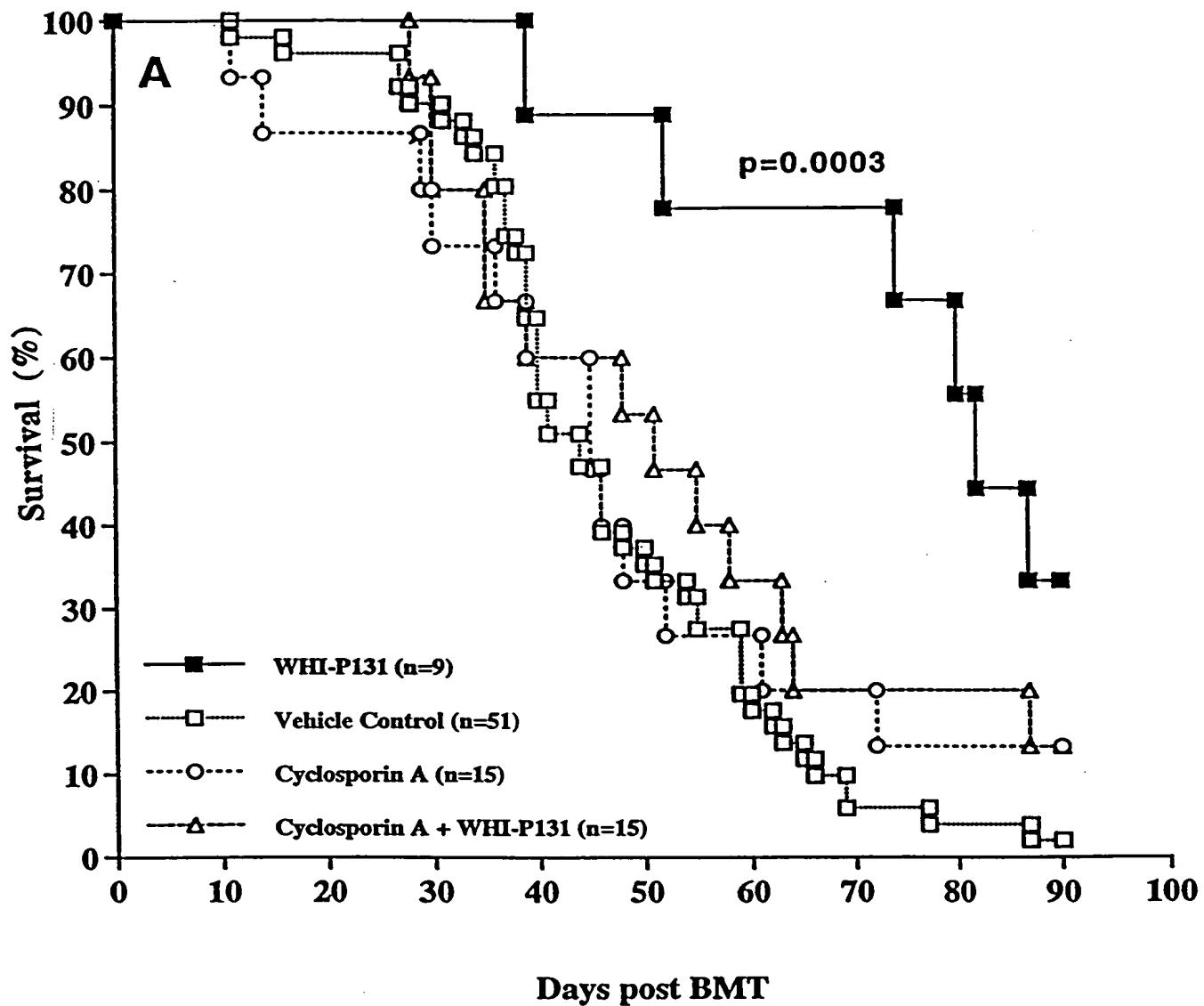


FIG. 24

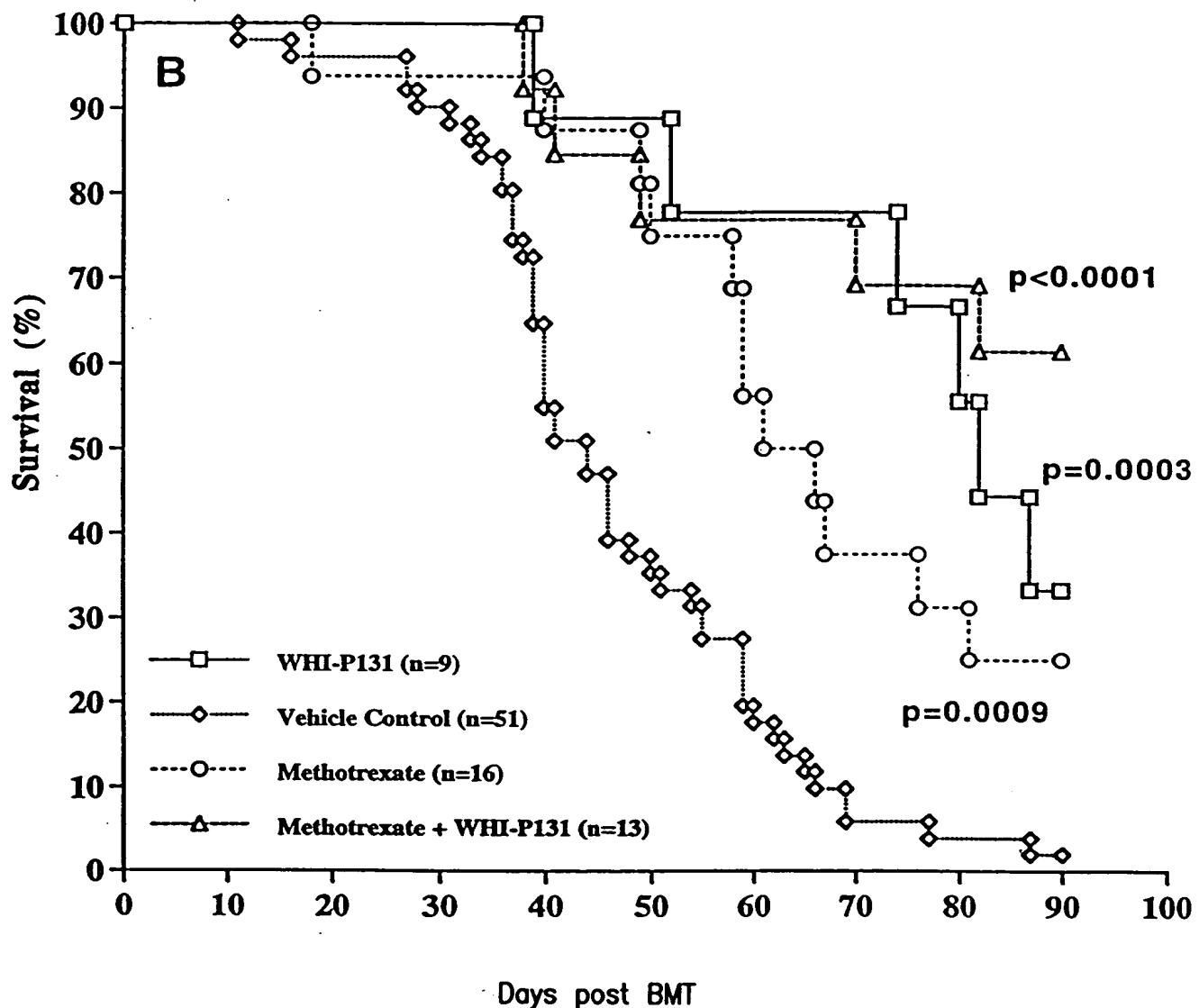


FIG. 25

**WHI-P131 (60 mg/kg/day) - effects on GVHD development**

**Cumulative proportion surviving**

<u>Group</u>	<u>n</u>	<u>Cumulative proportion surviving</u>		<u>median survival (d)</u>	<u>Logrank p value</u>	<u>Control vs. WHI-P131</u>
		<u>30</u>	<u>90</u>			
<b>CONTROL</b>	51	90.2 $\pm$ 4.2	17.6 $\pm$ 5.3	2.0 $\pm$ 1.9	44	
<b>WHI-P131</b>	9	100 $\pm$ 0	77.8 $\pm$ 13.9	33.3 $\pm$ 15.7	82	0.0003
<b>WHI-P132</b>	9	88.9 $\pm$ 10.5	11.1 $\pm$ 10.5	0 $\pm$ 0	44	0.485
<b>Methotrexate</b>	16	93.8 $\pm$ 6.1	56.2 $\pm$ 12.4	25.0 $\pm$ 10.8	63.5	0.0009 0.356
<b>Methotrexate + WHI-P131</b>	13	100 $\pm$ 0	76.9 $\pm$ 11.7	61.5 $\pm$ 13.5	87	<0.0001 0.320
<b>Cyclosporine A</b>	15	73.3 $\pm$ 11.4	26.7 $\pm$ 11.4	13.3 $\pm$ 8.8	45	0.493 0.029
<b>Cyclosporine A + WHI-P131</b>	15	80.0 $\pm$ 10.3	33.3 $\pm$ 12.2	20.0 $\pm$ 10.3	51	0.198 0.067

Methotrexate vs.  
Methotrexate + WHI-P131  
0.062

**FIG. 26**

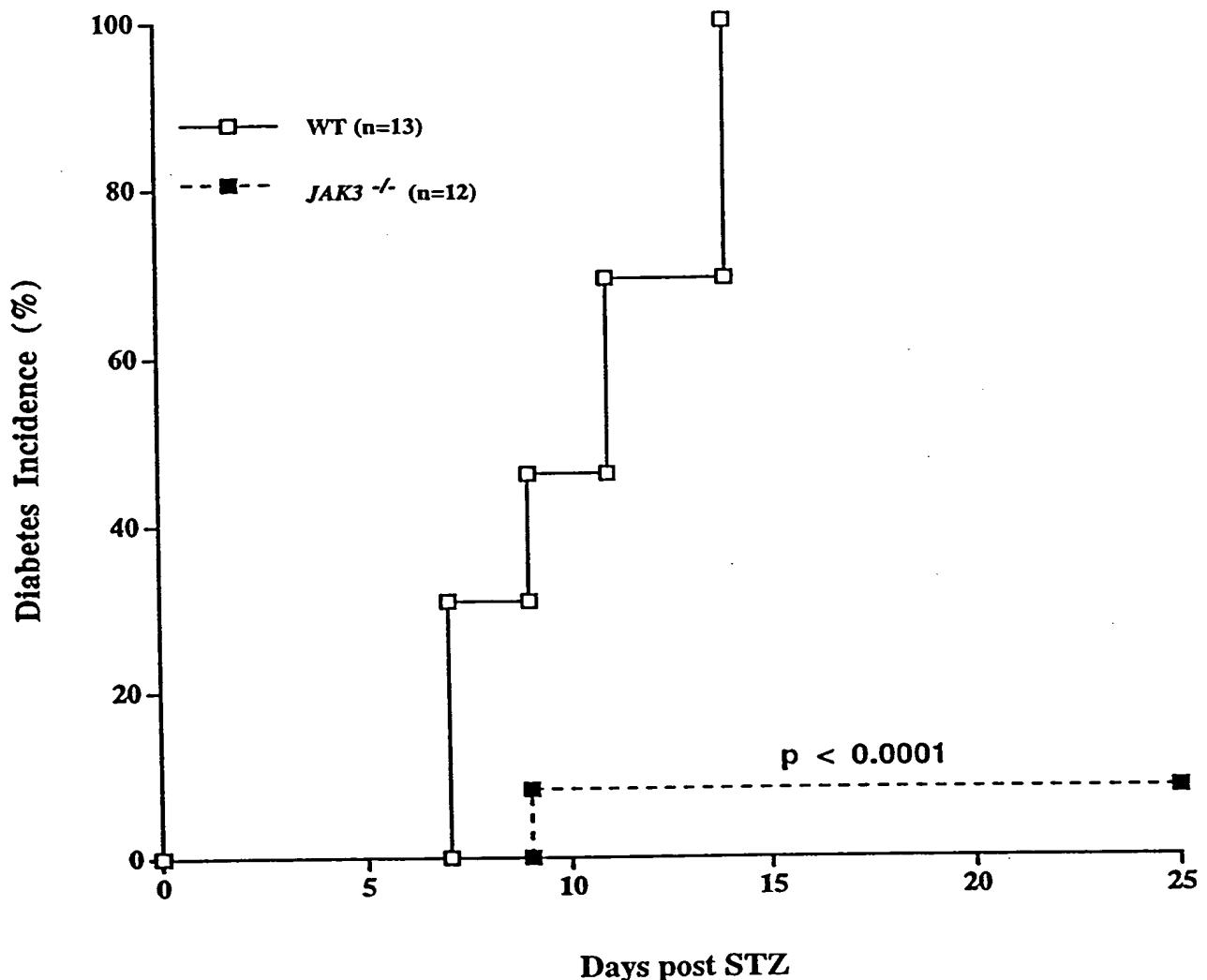


FIG. 27

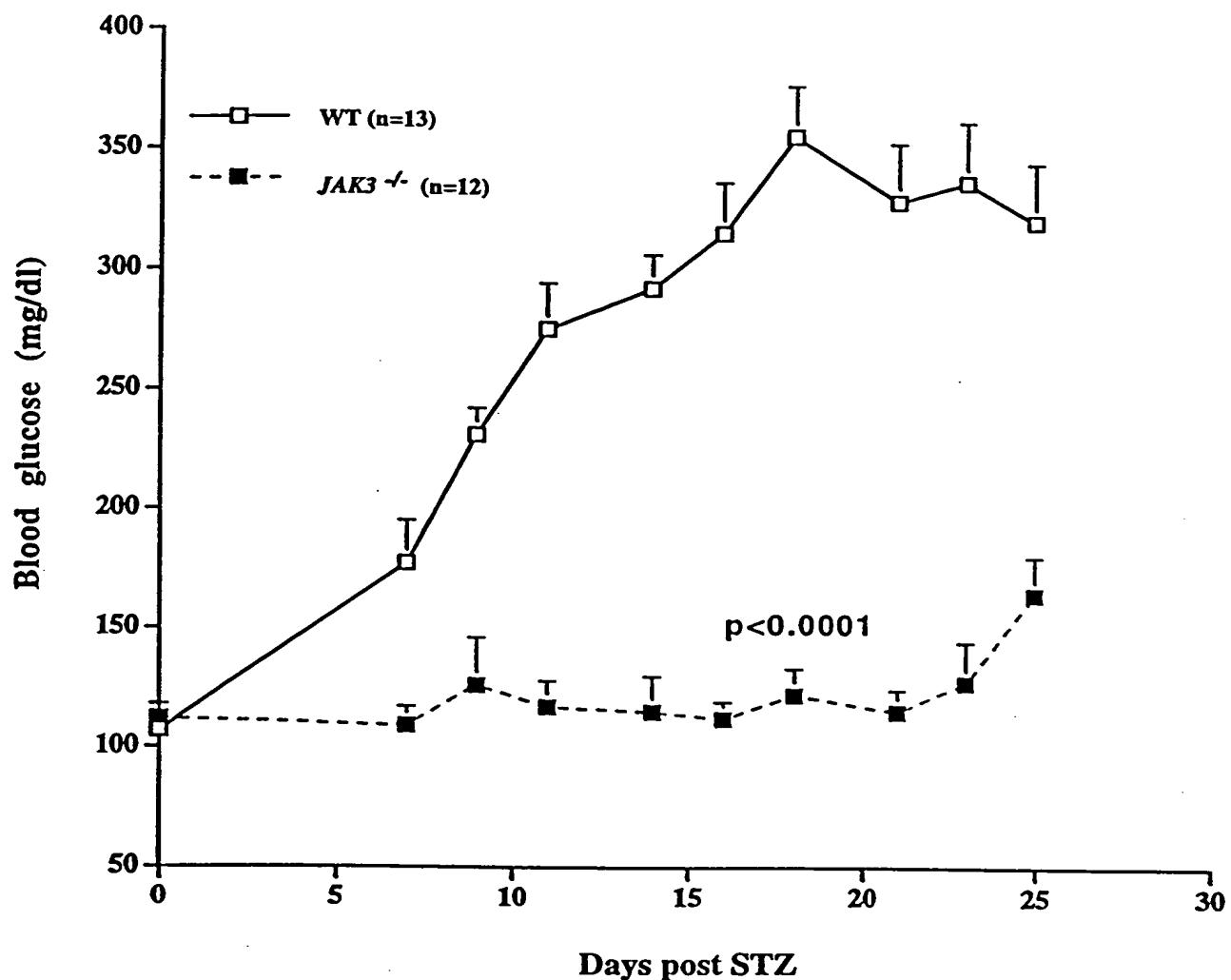


FIG. 28

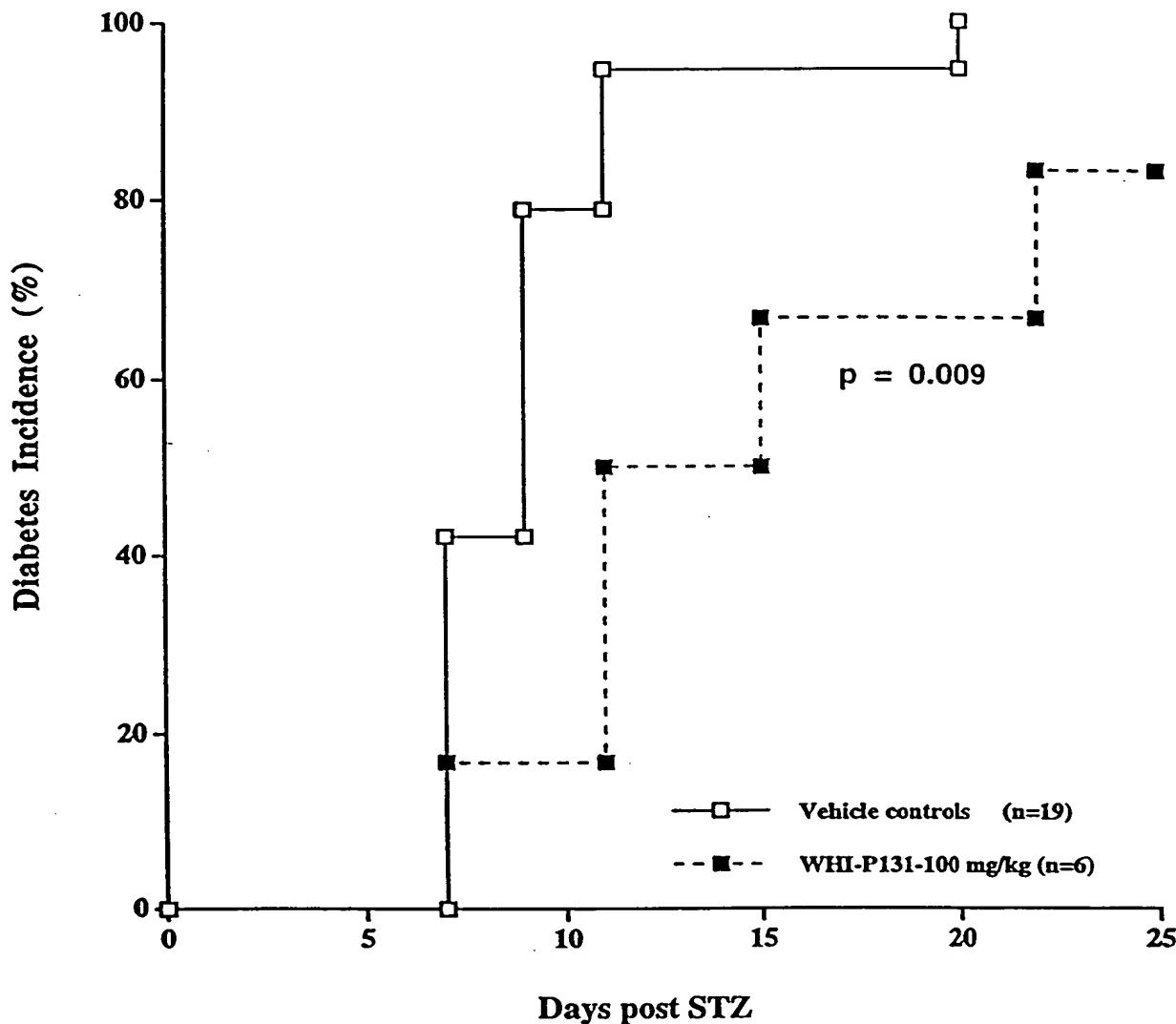


FIG. 29

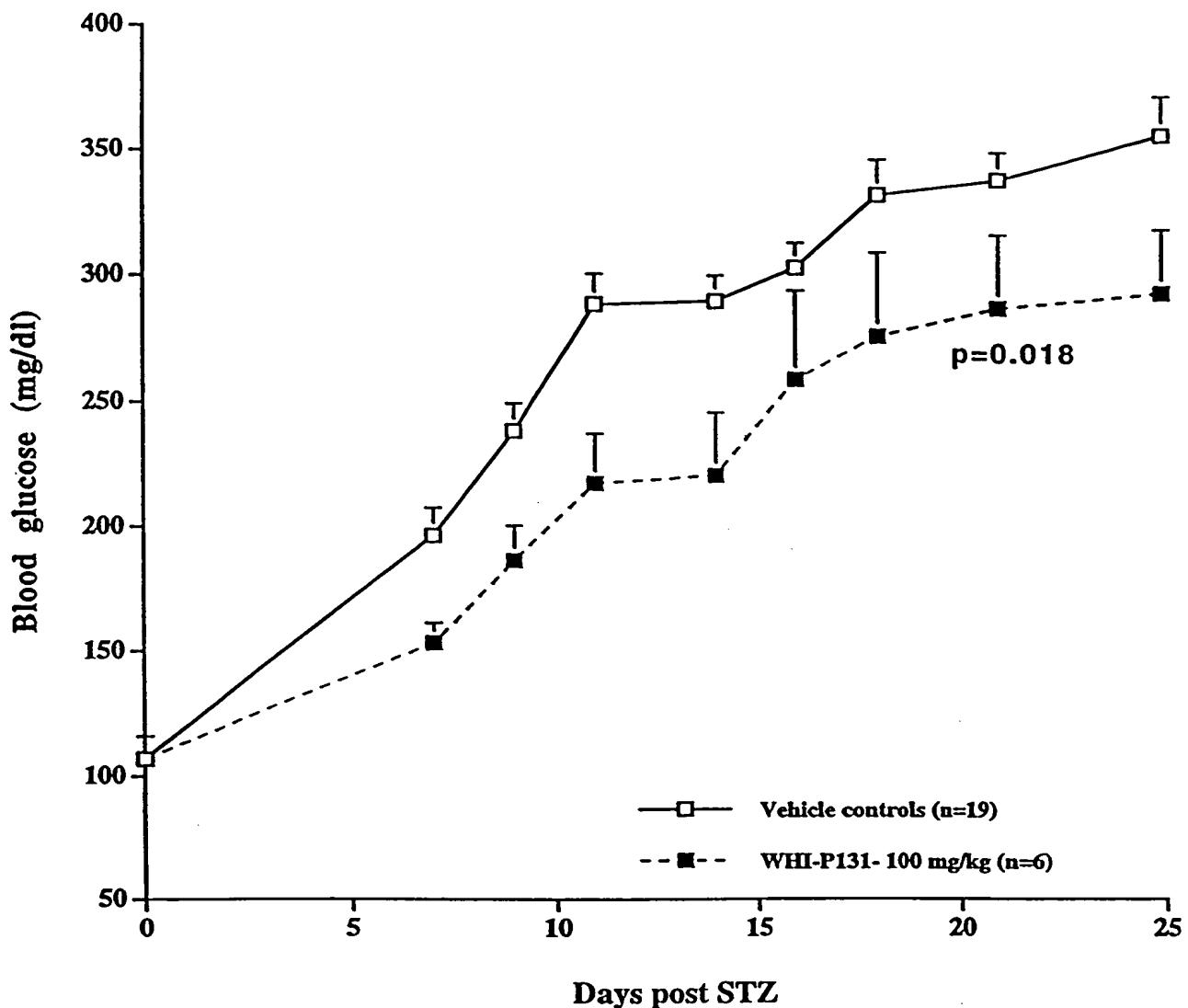


FIG. 30

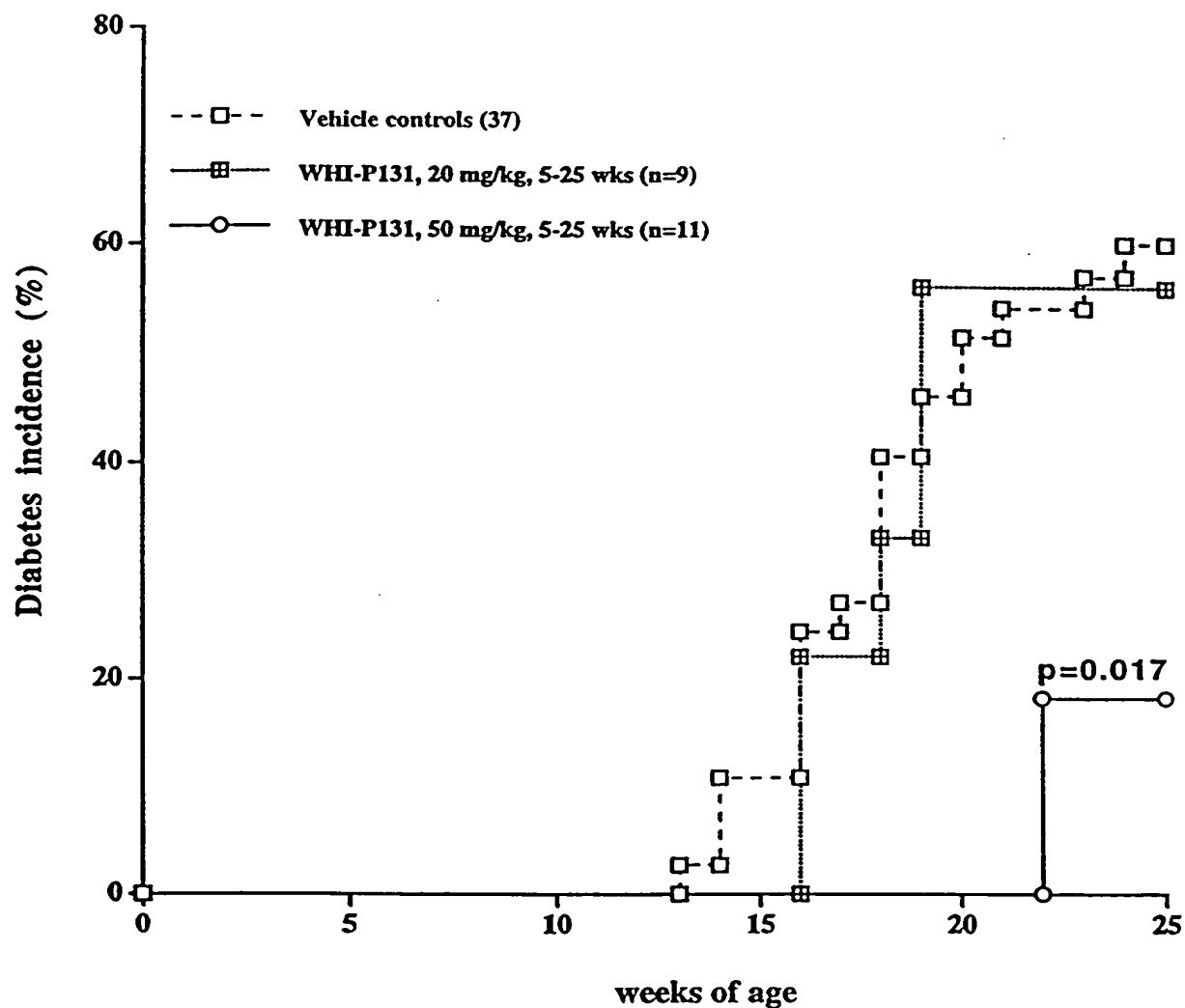


FIG. 31

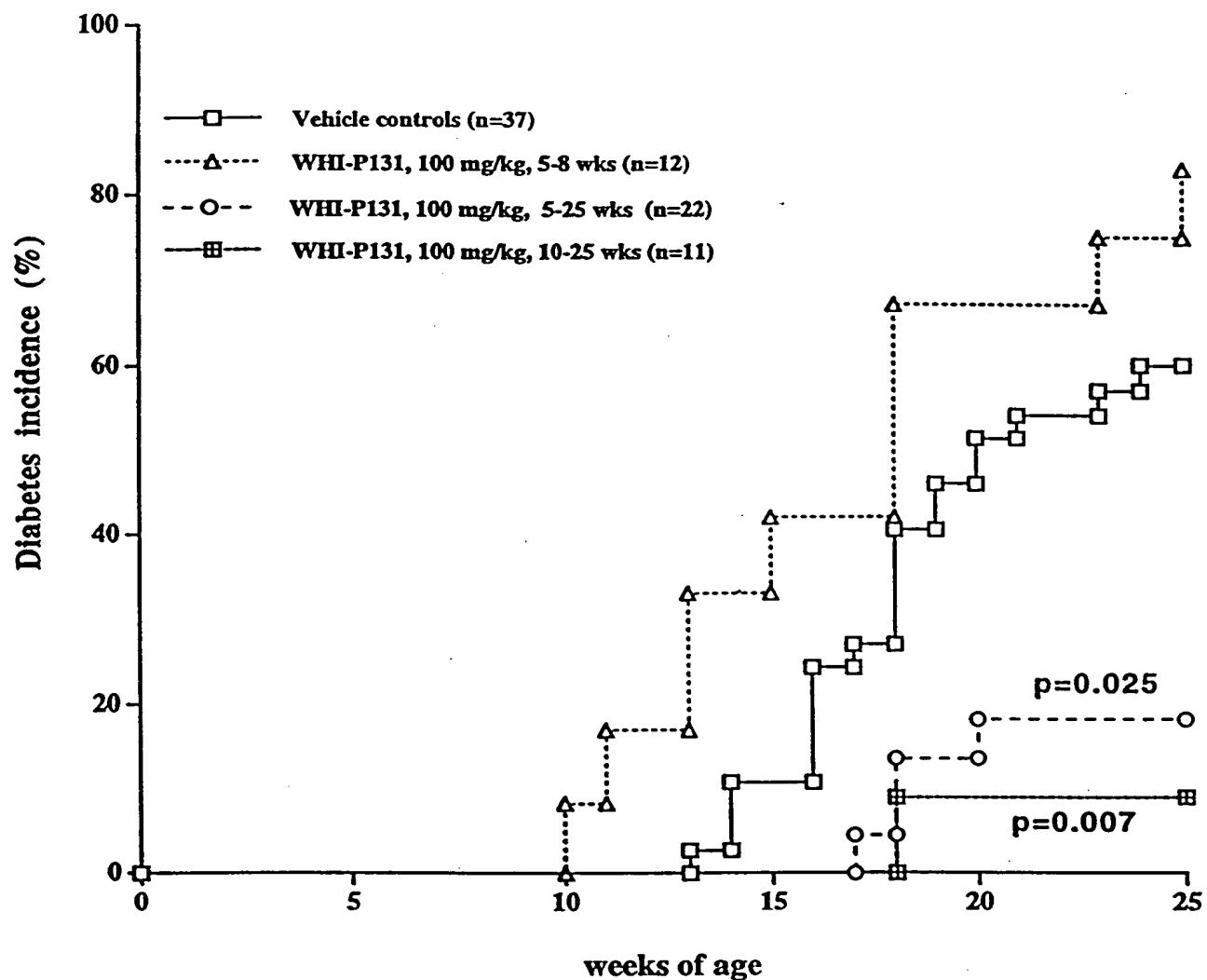


FIG. 32

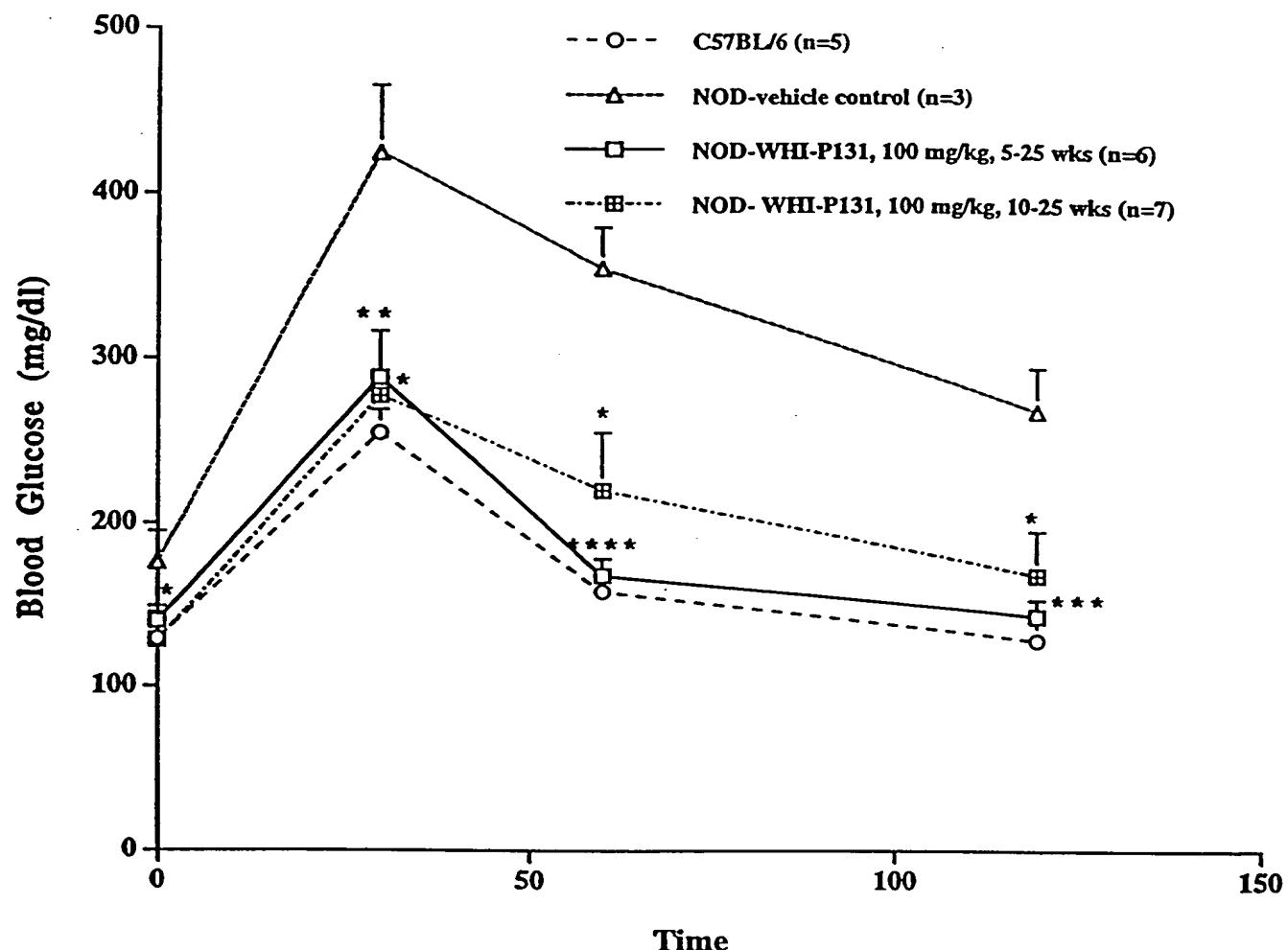


FIG. 33

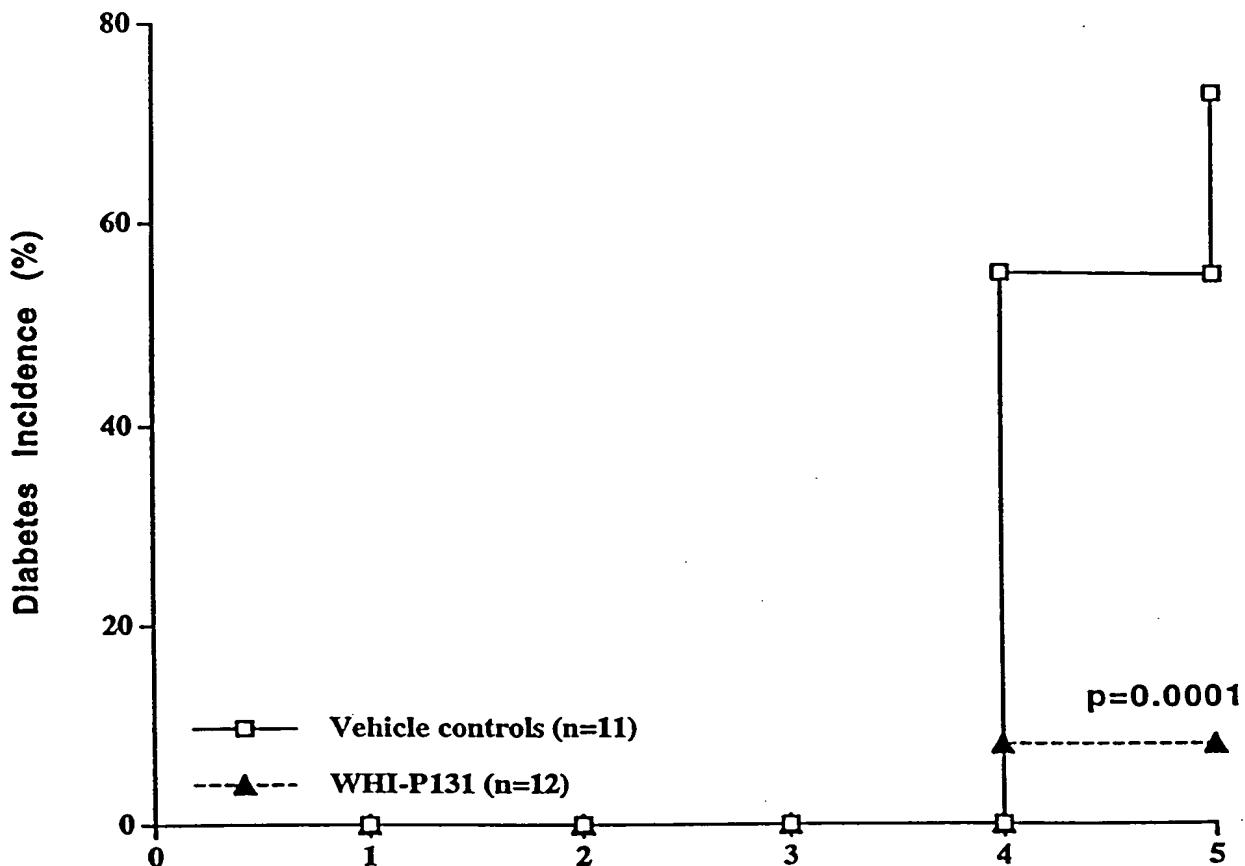


FIG. 34

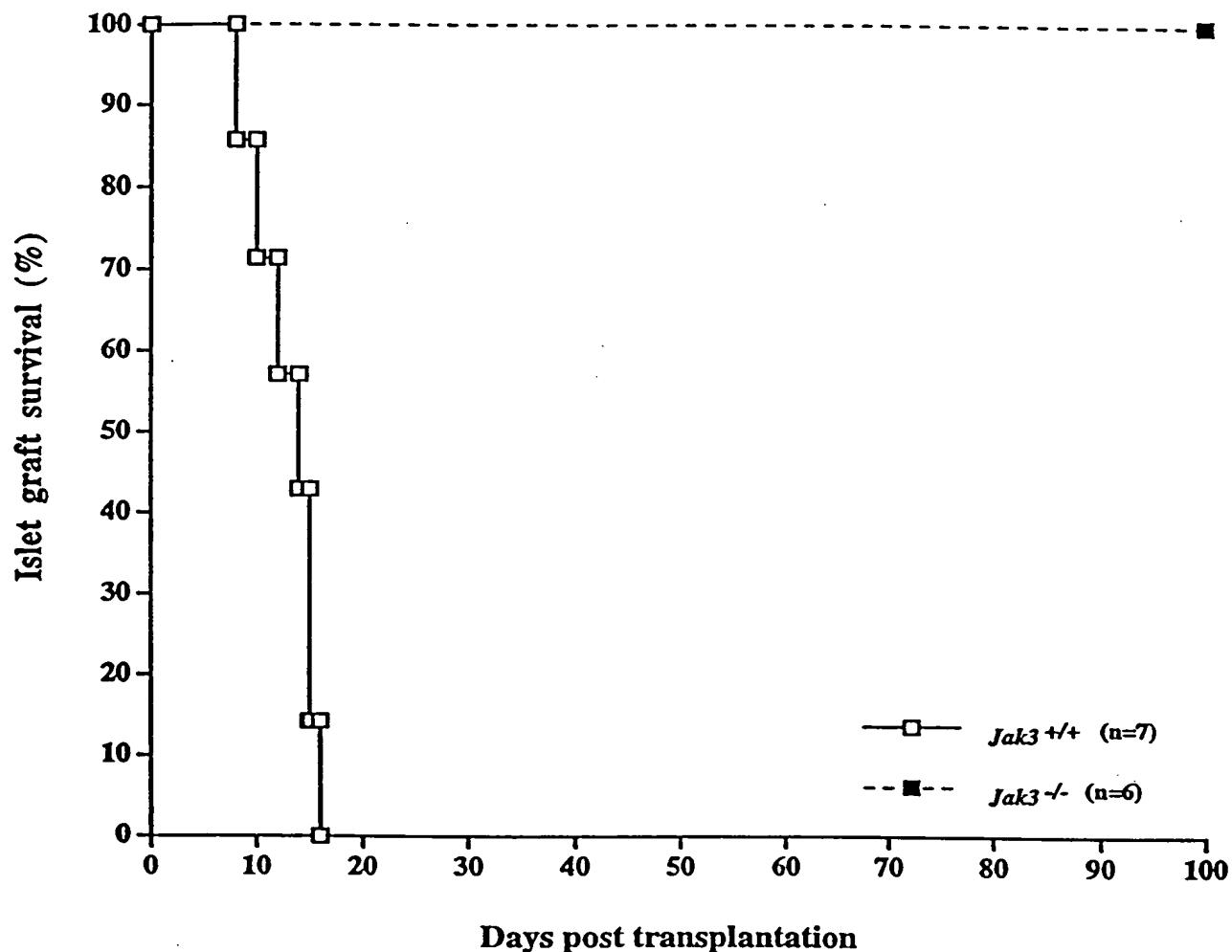


FIG. 35

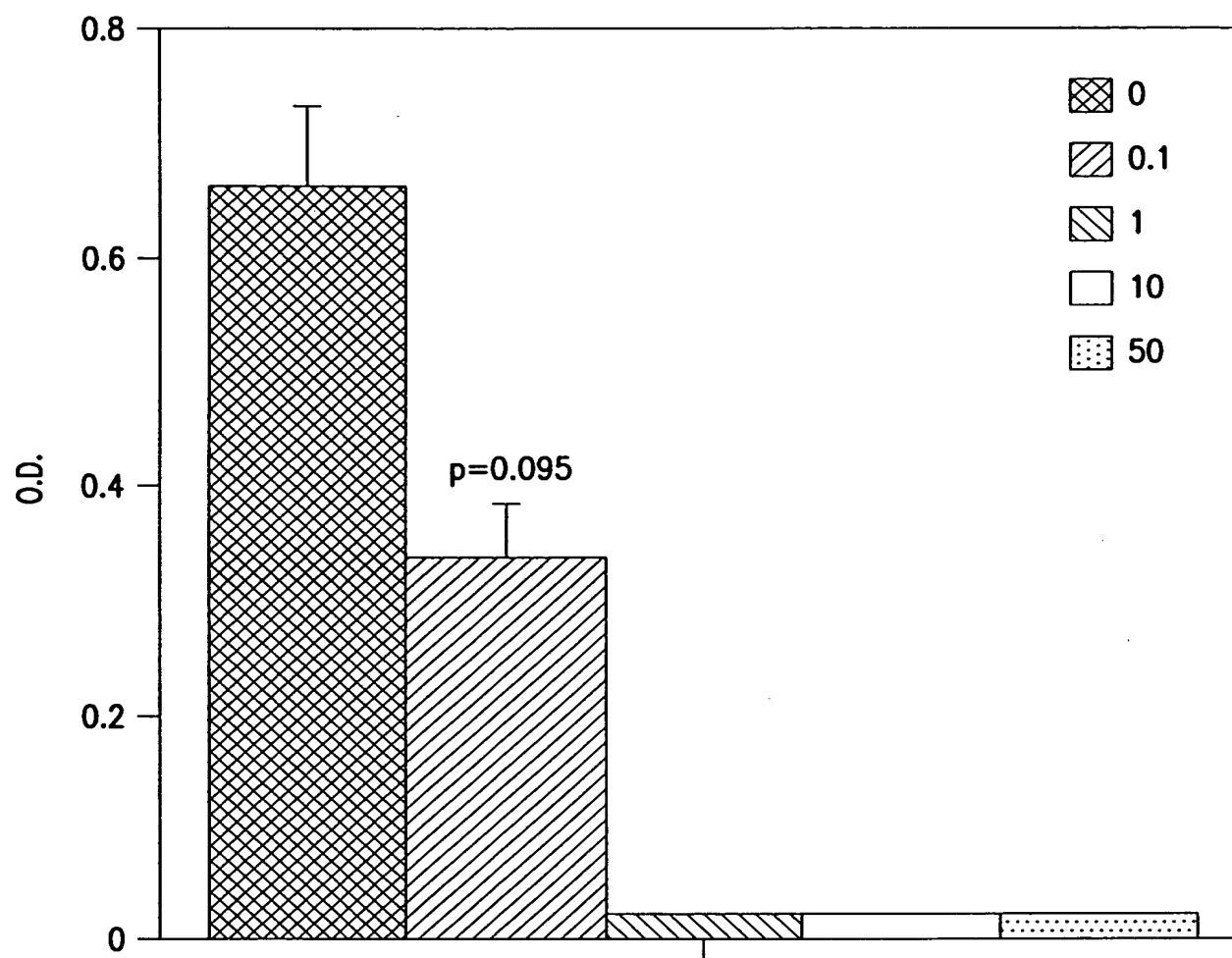


FIG. 36

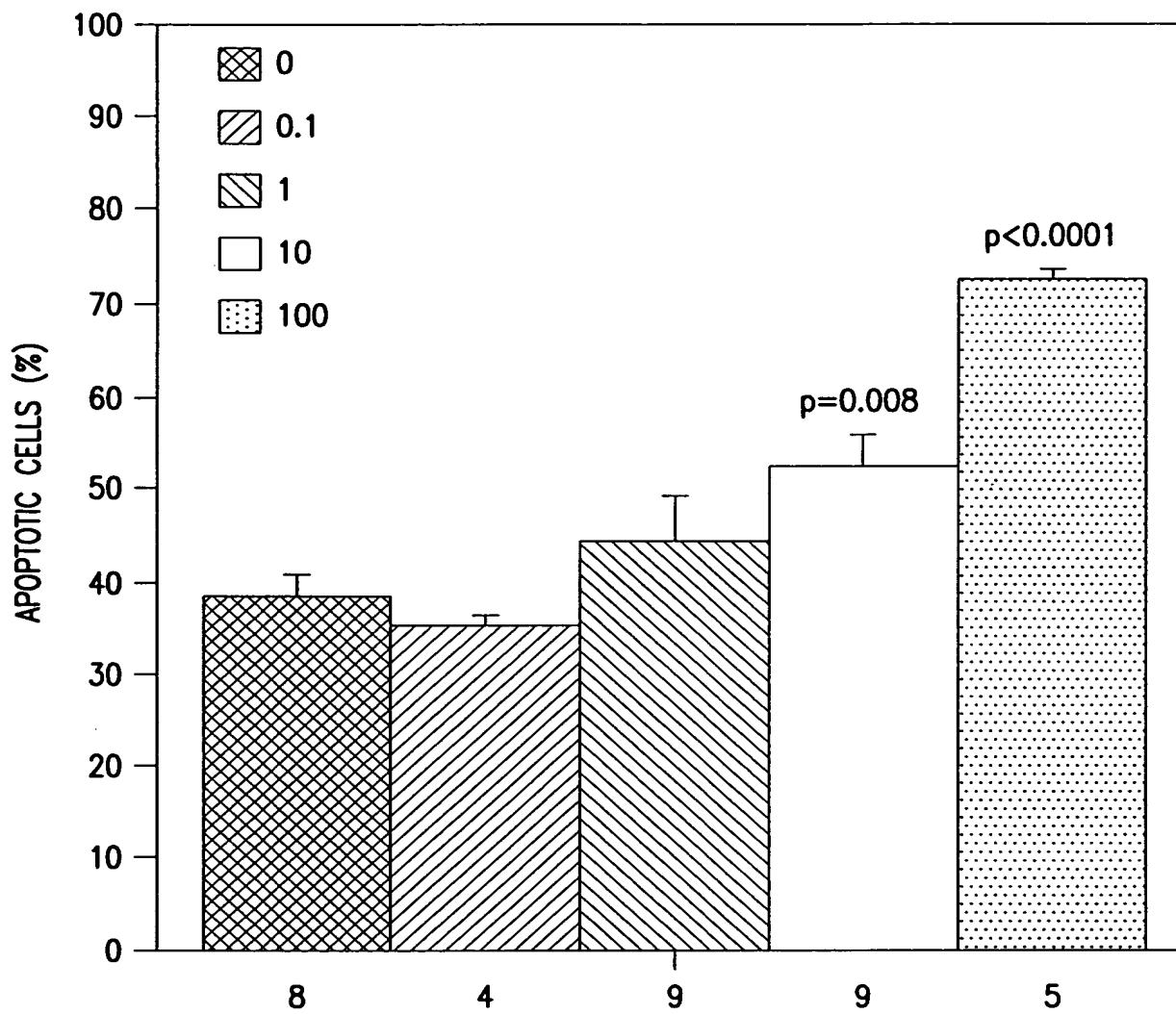


FIG. 37

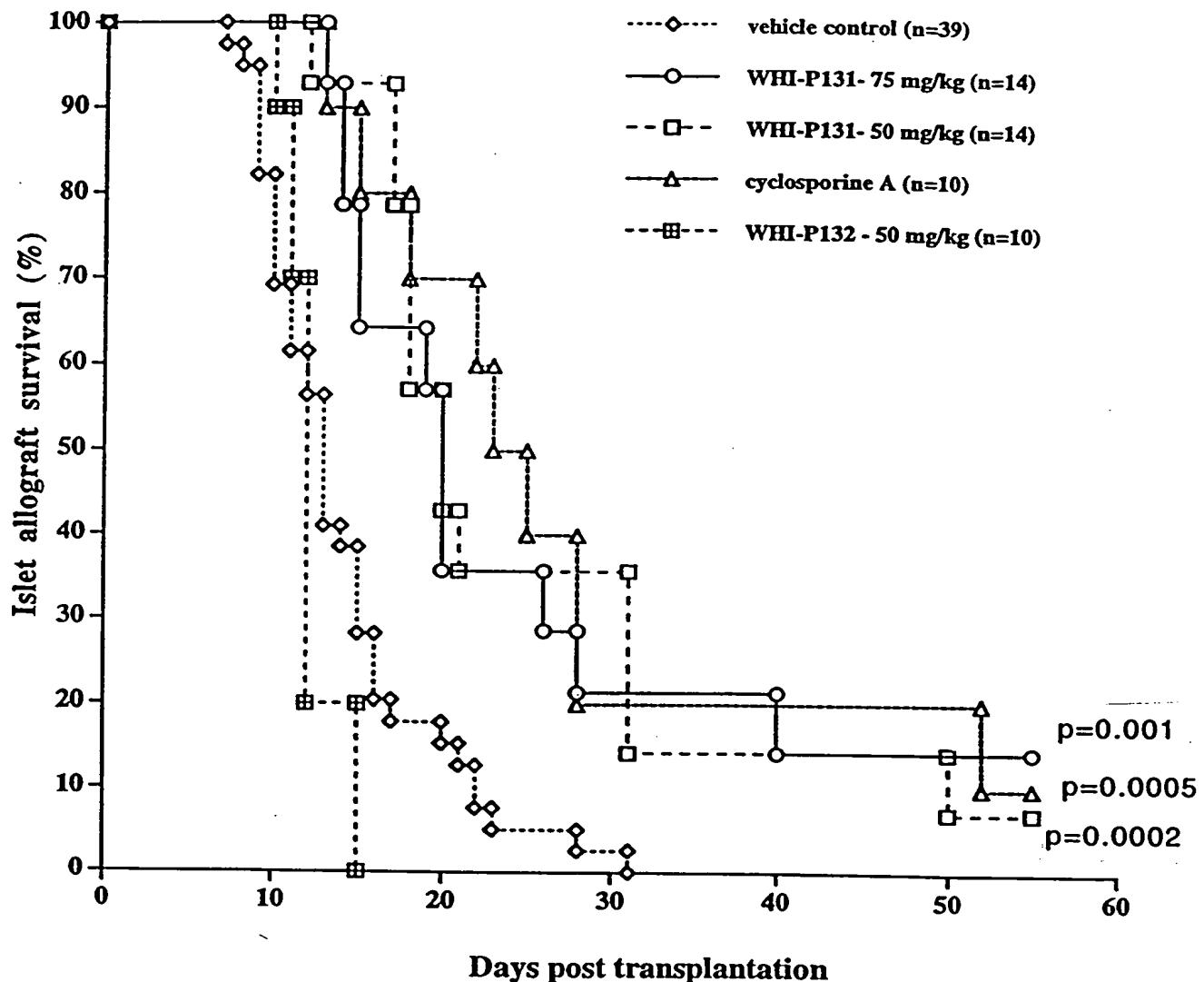


FIG. 38

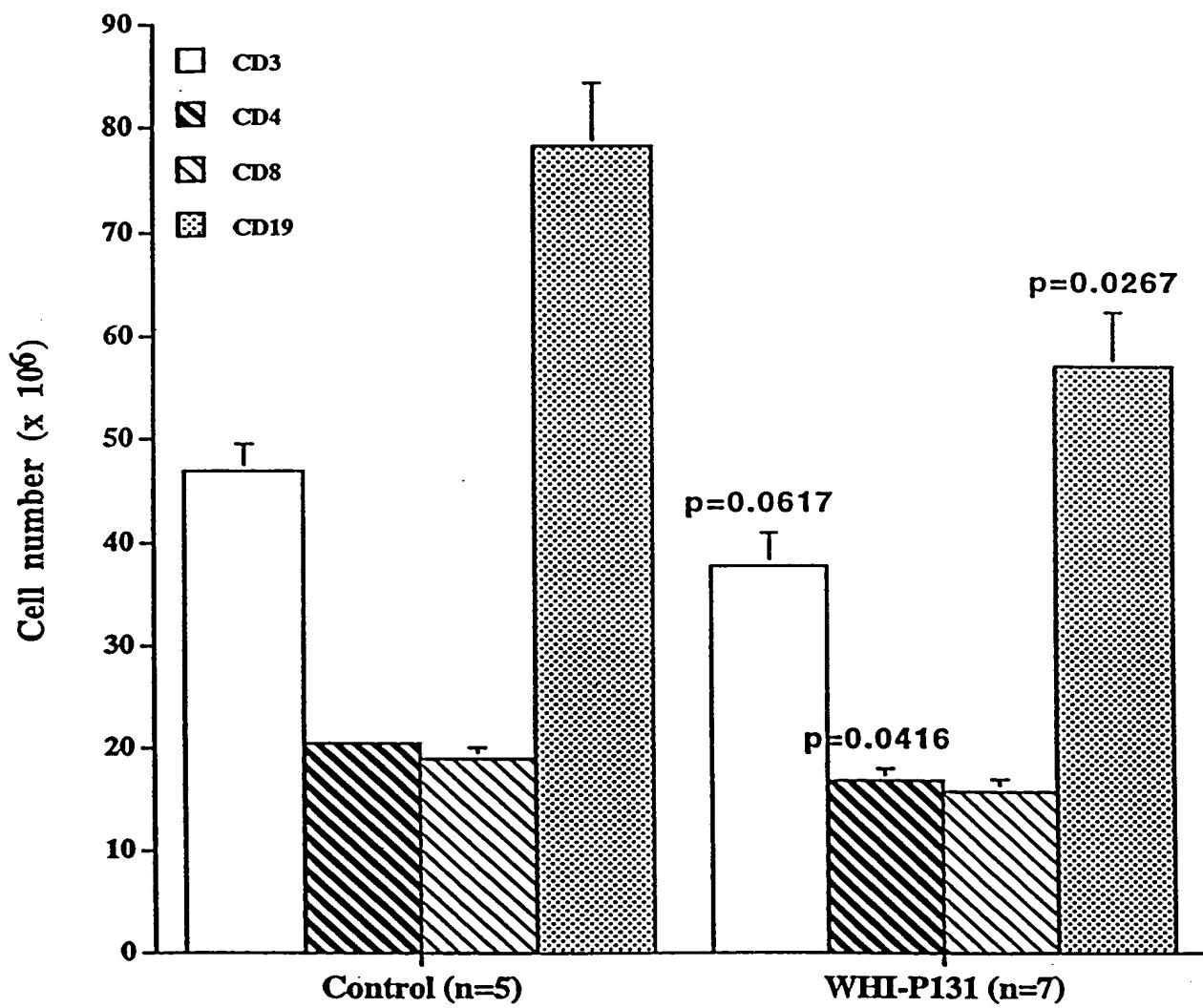


FIG. 39

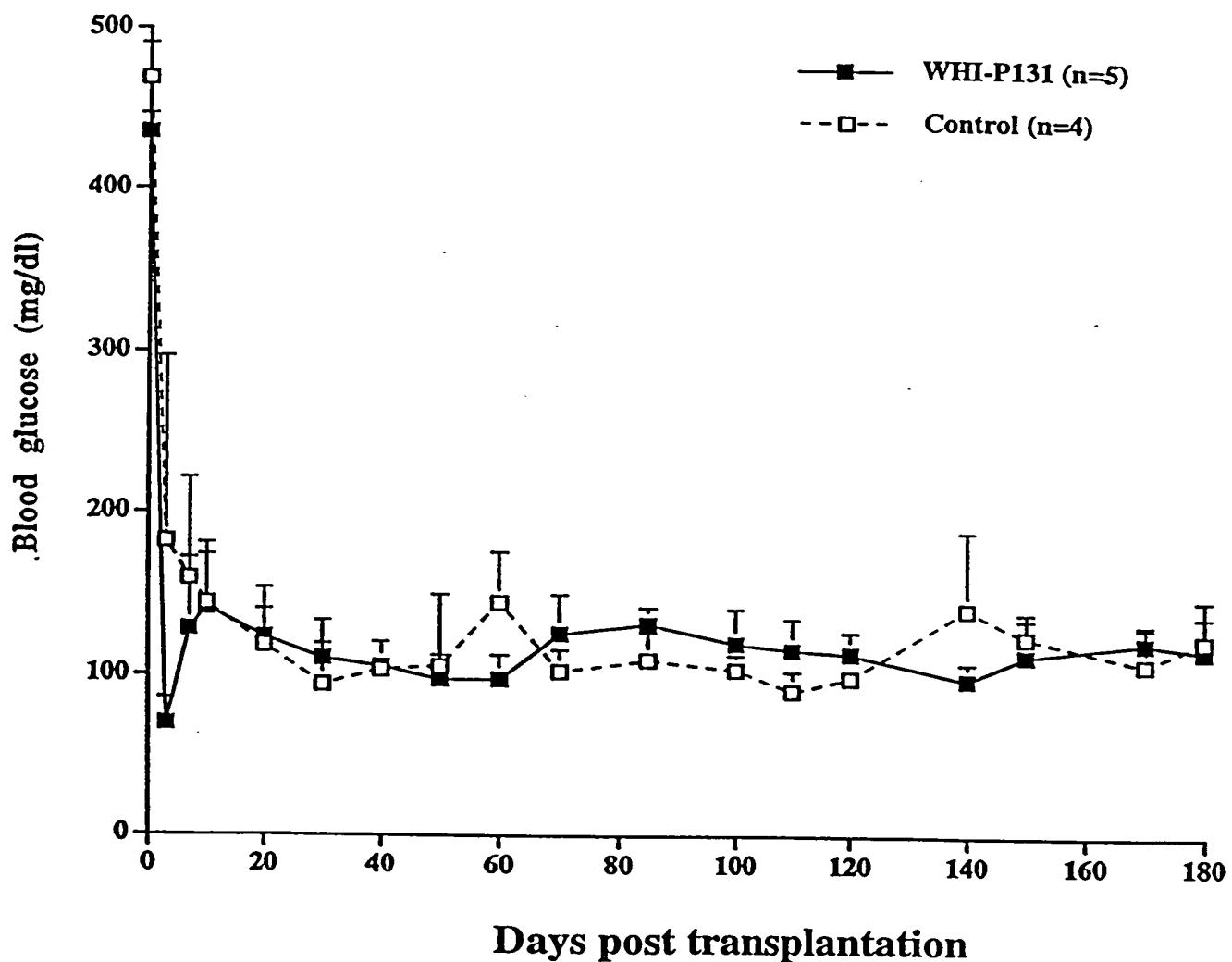


FIG. 40

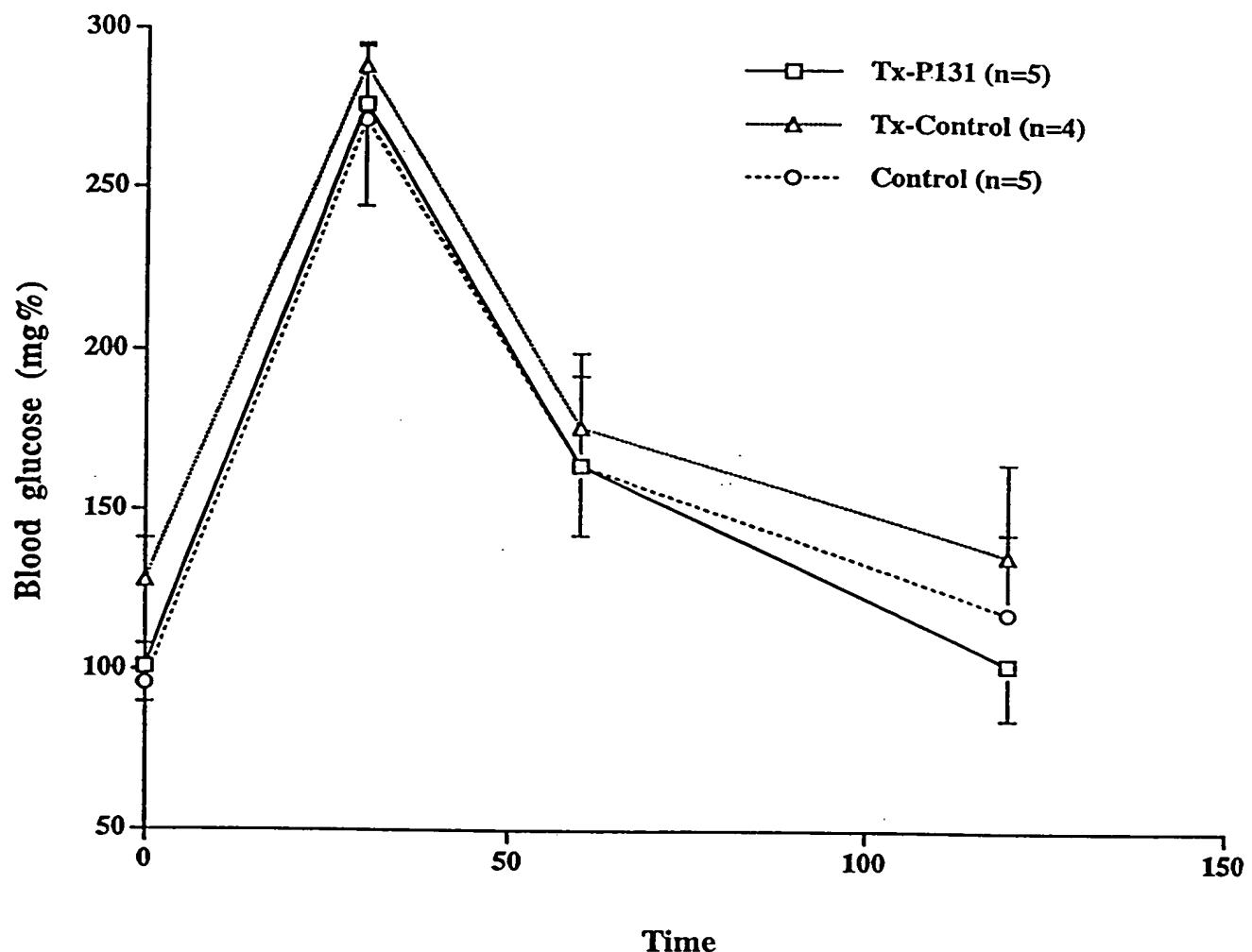


FIG. 41

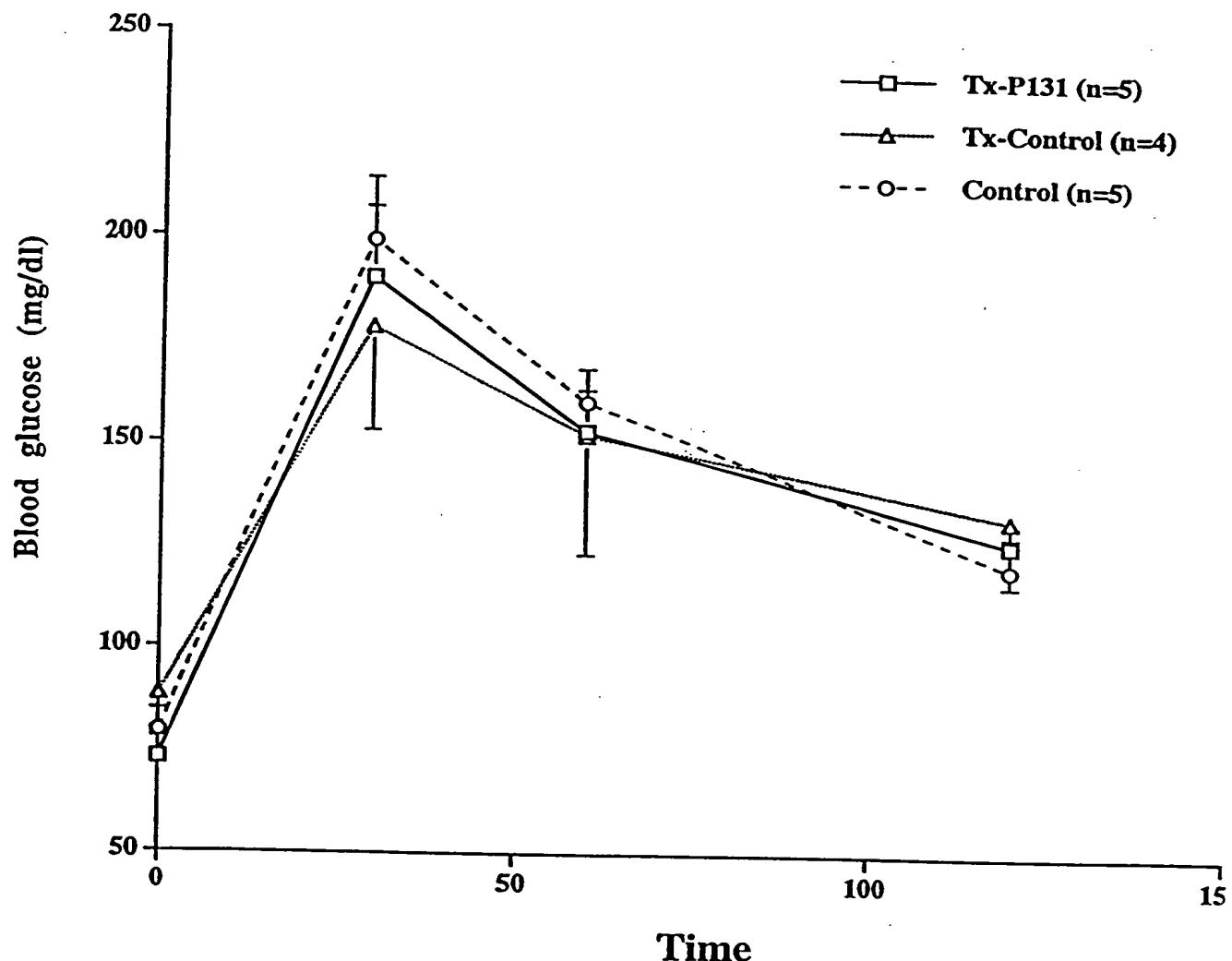


FIG. 42